THE American Journal OF Gastroenterology

VOL. 23, NO. 5 MAY, 1955

The Management of Instrumental Perforation of the Esophagus

Bleeding Esophageal Varices

Some Practical Considerations of Massive Gastrointestinal Hemorrhage

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Cirrhosis of the Liver: Its Relationship to Cholesterosis of the Gallbladder, Gallstones and Other Conditions

Retention Cyst of Liver Caused by Opisthorchiasis Associated with Carcinoma

The Surgical Treatment of Chronic Relapsing Pancreatitis

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The Pioneer Journal of Gastroenterology, Proctology and Allied Subjects in the United States and Canada

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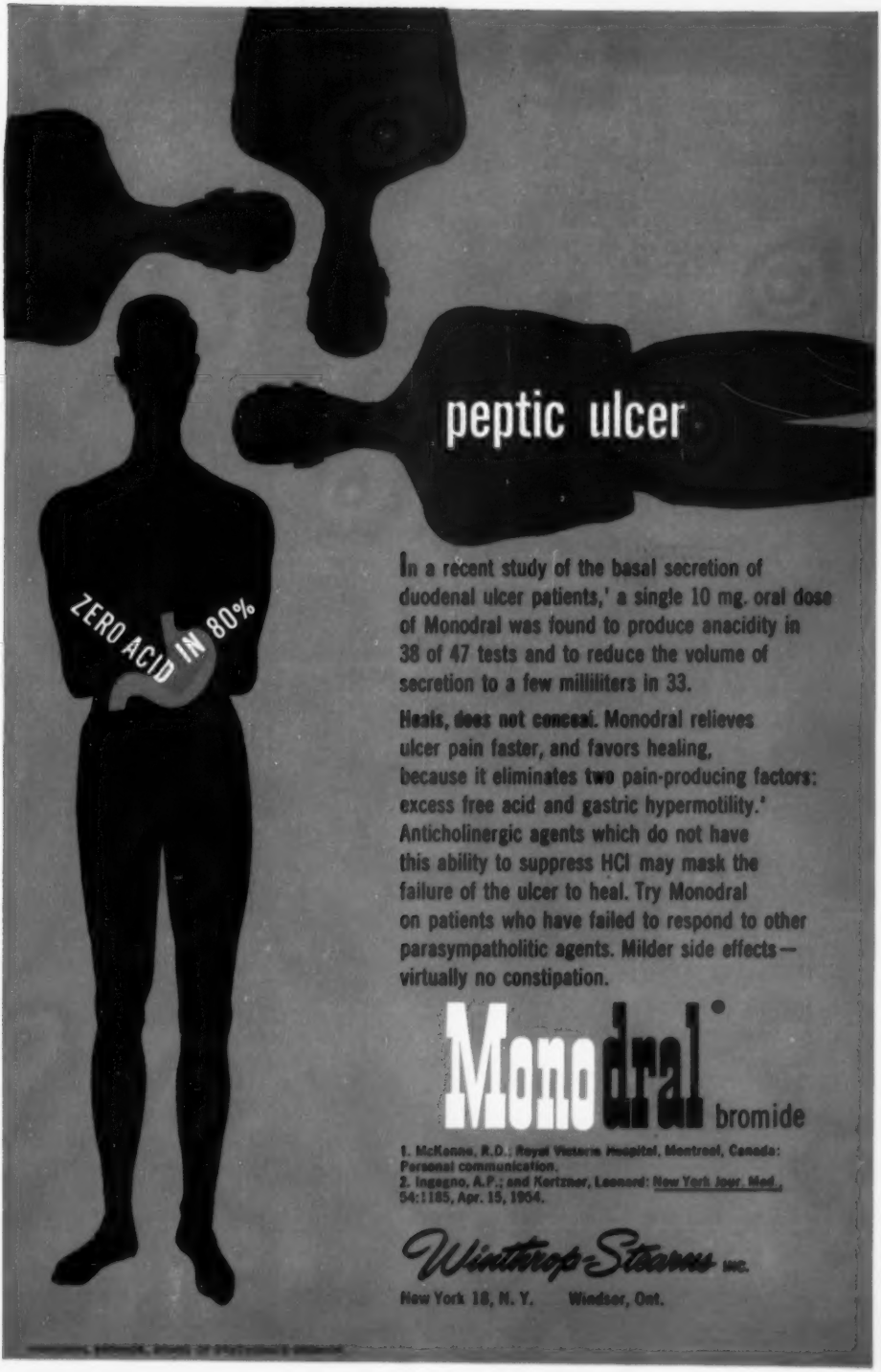

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1. McKenna, R.D.: Royal Victoria Hospital, Montreal, Canada: Personal communication.
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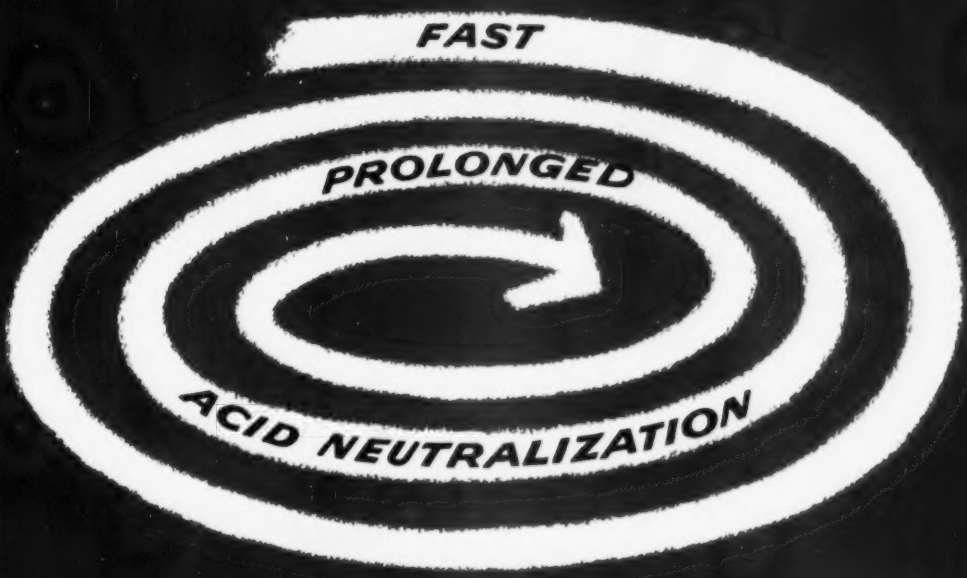

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2. Jankelson, I. R.: Am. J. Digest. Dis. 14:11 (Jan.) 1947.

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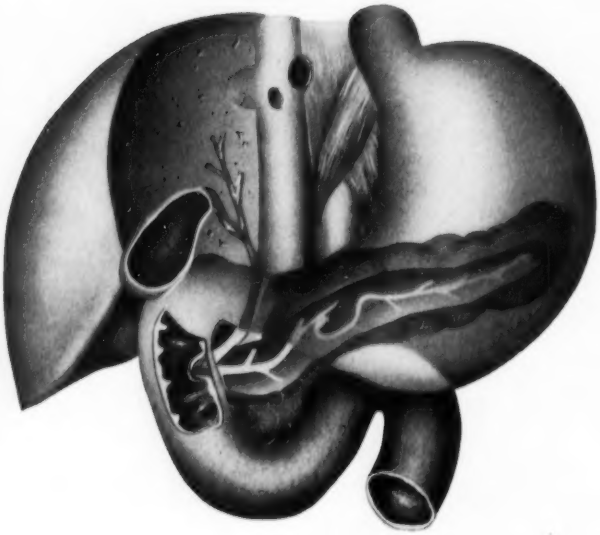

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THE American Journal OF Gastroenterology

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VOLUME 23 MAY, 1955 NUMBER 5

THE MANAGEMENT OF INSTRUMENTAL PERFORATION OF THE ESOPHAGUS*

JOHN TILDEN HOWARD, M.D.

Baltimore, Md.

In the autumn of 1946[1] I chided a gathering of gastroenterologists about "the dismemberment of the gastrointestinal empire". I said, "Some gastroenterologists have not been conscious of the partitioning of their domain by the roentgenologists, the parasitologists, the proctologists, and the otolaryngologists. So frequently has the gastroenterologist asked for the help of these specialists that he, too often, has become dependent upon them; he finds himself referring his patients to the parasitologist for microscopic examinations which he or his technician might do (or be trained to do), to the proctologist for inspection of the rectum and lower sigmoid, to the roentgenologist for skiagraphic studies of the gastrointestinal tube, and to the otolaryngologist for endoscopic examination of the esophagus." I urged my fellows to beware lest they become mere clerks who refer patients to this or that specialist who may be working in a field that is actually within the gastroenterologist's domain, a domain in which he himself should be competent. In that talk I called particularly for the re-annexation of the esophagus to our realm, a position which it originally had in Europe, and perhaps in this country, before the otolaryngologists took it over. With technical advances and studies admittedly of the greatest value, the nose-and-throat men had quietly and surely extended their boundaries beyond the head and neck into the bronchi, into the esophagus, and even into the stomach. I could manage the gastroscope quite well but I felt somewhat inadequate in my inability to perform esophageal procedures until I had learned what others had learned before and more have learned since, that the passage of the stiff esophagoscope could be facilitated by the use of a flexible rubber obturator. This obturator (Fig. 1) when passed through the Jackson 'scope opened the tight cricopharyngeal constrictor muscles quite easily when the head was held in the Jackson "high-low" manner and it frequently facilitated the passage of the 53

*Read before the First Annual Convention of the American College of Gastroenterology, Washington, D. C., 25, 26, 27 October 1954.

cm. instrument into the stomach! I was so delighted with what I called my Adventures in the Esophagus that I had to tell my fellows about my inspections of gullets, my dilatations of cardias, my stretching of strictures, etc. I said that the instruments of this day with a gentle hand should enable the gastroenterologists to recover their lost territory, the esophagus, for diagnosis and nonsurgical therapy and I urged these men to enter their traditional field. Probably I then minimized the dangers of the procedures for I had had no accidents. Older now and more experienced, I wish to recount some of my sobering, but not disheartening, "adventures" (accidents) for those gastroenterologists who may be doing, or who may be contemplating doing, esophageal work.

I began to do esophageal procedures in 1941 and it was seven years later that I had my first instrumental difficulty.

Case 1:—Mrs. J. T. R. (J. H. H. No. 450922) had been seen by me in the Hospital's Diagnostic Clinic for an esophagoscopic examination several weeks

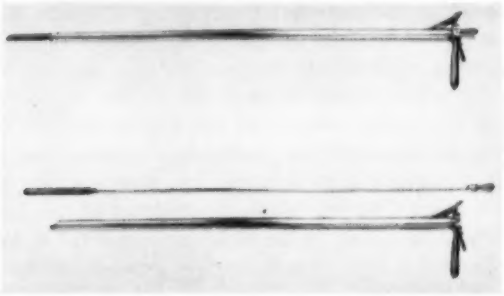

Fig. 1—Jackson esophagoscope and homemade rubber-tipped obturator. The rubber end fits the instrument's lumen rather snugly.

before I saw her in my office in March of 1948. In the Clinic her diagnosis had been cardiospasm and psychiatric treatment had been suggested because treatment with a pneumatic dilator in another city had done her no good and since she had many anxieties. The patient's cousin, a physician in Baltimore, sent the lady to me in March of 1948 because she was rapidly losing weight and strength; as he put it, "Something must be done for her dysphagia!" And I did it, as you'll see.

Mrs. R. came to my office frightened but desperate. She weighed 96 pounds and she was poorly muscled. Before the fluoroscope the Tucker cardiospasm dilator was passed. When it had been properly positioned, it was inflated to a pressure of 6 pounds twice and once to that of 9 pounds. The patient complained of a good deal of pain during the dilatation but, after resting a half-hour, she left the office with her physician-cousin, who had watched the procedure.

Five hours after the dilatation the patient telephoned me to say that an hour before her call she had developed severe pain in her lower chest on the left and under the costal margin on that side. One hour after the telephonic conversation I saw the patient. She was doubled up with pain; the left upper quadrant of the abdomen was board-like and tender; the leucocytes were 20,900 and the temperature was 97.7°. She was sent into the Hospital where she was fed intravenously and where she was given penicillin. Nine hours after the instrumentation the temperature was 99.5° and the white cell count was 21,000; films of the abdomen and chest were unrevealing. The day after dilatation the leucocytes were 10,200 and she was given a liquid diet. This she took well and she left the Hospital against advice five days after the esophageal tear.

In August of this year Mrs. R. consulted me "on general principles". She was 14 pounds above her weight in 1948 and she had no subjective dysphagia. The previously dilated gullet was of normal size and it showed incoordinated

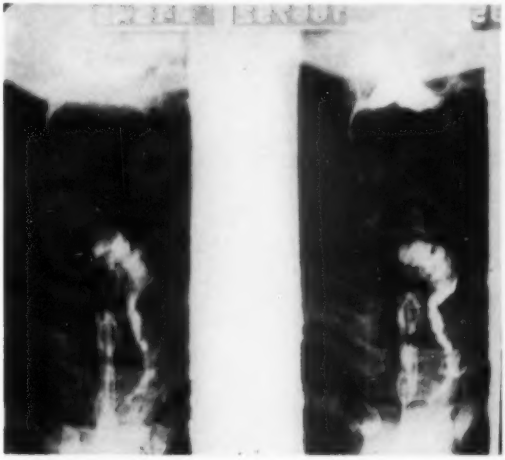

Fig. 2—Barium running into soft tissues of neck after instrumental perforation of the cervical esophagus.

contractions but there was no real obstruction. The patient continued to be tense subjectively and in her appearance.

Case 2:—Mrs. M. S. (J. H. H. No. 166752) was my first esophagoscopic "casualty". She was referred for that procedure and for gastroscopy in February of 1949 because of persisting dyspepsia, pain in the chest, and the passage of tarry stools. Skiagrams had shown a short esophagus with a thoracic stomach and a duodenal ulcer.

The patient was a small thin woman who weighed 95 pounds and whose musculature was not good. When I tried to pass the rubber obturator of my esophagoscope through the constrictors of this patient's pharynx, I was unable

to do so easily and finally I gave up the attempt with the notation on her record, "We'll have her upper esophagus re-examined with the x-ray today and I'll try endoscopy again later. It's better to be careful than sorry." I spoke reassuringly to the patient, for I didn't believe that anything serious had happened. I told her to return to her home after the roentgen examination and to get me on the telephone if she had temperature of consequence. She did call me about ten hours after the endoscopic session and she reported that her temperature was 102° and that the left side of her neck was swollen. I told the patient to meet me at the Hospital.

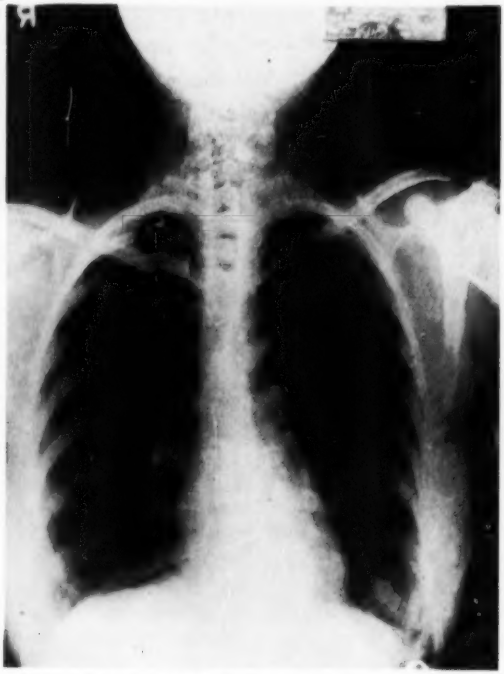

Fig. 3—Small diverticulum of cervical esophagus where it had been perforated and sutured two and a half years previously.

It was obvious when I saw the patient that she had inflammatory trouble on the left side of her neck. The temperature had risen to 103° and the leucocytes were 15,000. The films which had been made that afternoon were gotten out and they showed a very definite leak from the gullet into the soft tissues of the neck (Fig. 2). There was no subcutaneous emphysema.

I was glad, very glad, that we have surgeons and I called for their help. The hole in the esophagus was sutured that night, the barium about the rent was aspirated, and the wound was drained.

The postoperative treatment was feeding through a Levin tube for twelve days and the use of penicillin and of streptomycin. In spite of suturing and antibiotic therapy a fistula between the esophagus and the skin of the neck developed and it drained saliva. But this closed gradually and the Levin tube was kept in place until it had closed completely.

Mrs. S. had a little trouble swallowing when she returned in the autumn of 1949 but her main complaint was epigastric pain and nausea and hematemesis.

Fig. 4—Obstructive lesion in mid-esophagus of patient in whom the esophagoscope could not be passed and who had mediastinitis eight days after unsuccessful endoscopy.

In March of 1950 she had a high subtotal gastric resection and her upper abdominal symptoms were relieved.

Her dysphagia increased, however, and she had to limit her diet to liquids and to the softest foods. She weighed 97 pounds in July of 1951. Films of her esophagus at that time showed a small diverticulum just below the larynx and at the site of the instrumental perforation (Fig. 3). I suppose that the lady said, "Though he slay me, yet will I trust him" or she was desperate for a good steak. At any event, in August of 1951 with the idea that there might be a cicatricial stricture of the gullet as well as a diverticulum, she swallowed a

thread and she allowed me to pass metal beads of increasing size through her strictured esophagus before the fluoroscope. Fortunately for both the patient and myself all went well and when I next saw her in October of 1951 she weighed 105½ pounds.

Case 3:—Judge W. C. S., (J. H. H. No. 638548) aged 66, came to see me in April of 1953 because of dysphagia of one week's duration. Roentgen studies showed an obstructing lesion in the middle third of the gullet which was probably a cancer (Fig. 4). There was no lesion in the upper gullet or in the hypopharynx. I had no difficulty in persuading this jurist to have an esophagoscopic examina-

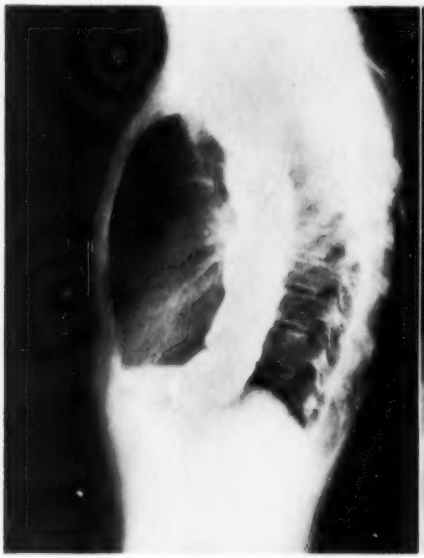

Fig. 5

Fig. 6

Fig. 5—Classical cardiospasm with a dilated gullet is shown. There was an esophageal tear when the cardia was dilated with a pneumatic bag before the fluoroscope.

Fig. 6—Lipiodol escaping into tissues of the thorax as well as entering the stomach. This occurred seven days after the therapeutic accident.

tion when I said that I wanted to establish his diagnosis "beyond reasonable doubt".

The subsequent day I was unable to pass the rubber obturator of the esophagoscope through the constrictors of the patient's pharynx. It appeared that I was putting the obturator in the proper place; it just would not pass on several attempts and I had to give up the procedure, ashamed because I had failed in it and because I had "beaten up" the patient's throat. The evening of the day of the endoscopic session I stopped at the patient's home because I was

a little worried about him. He had a temperature of 100.6° and a very sore throat. The neck was not swollen. I called the patient on the telephone for two days subsequent to his attempted endoscopy and while he reported a sore throat, he had no elevation of temperature and he went to his office daily. Eight days after the instrumental trauma to the patient's throat, he had a chill which was followed by a rise of temperature to 103°. Inspection showed a little swelling on the left side of the patient's neck and there was tenderness above the left clavicle. The patient was sent to the hospital where his leucocytes were found to be 14,800, where he was given nothing by mouth, and where therapy with penicillin and streptomycin was begun. The fever subsided in three days along with the supraclavicular swelling.

I felt certain that the patient should have a thoracotomy for the exploration of his esophageal lesion. The surgeon whom I called in thought that esophagoscopy should be performed and, since I was reluctant to attempt that again, he selected another endoscopist. I wouldn't be human if I didn't admit here that I was secretly pleased when my confrère could not pass his esophagoscope through the cricopharyngeal constrictors. He used a filiform bougie as a lumen-finder but the 'scope could not be gotten down.

It is possible that the carcinoma, which was later found at thoracotomy, leaked a little spontaneously and caused the fever and supraclavicular edema eight days after my manipulations. But I fear that that is wishful thinking and that there was more likely latent infection in the patient's neck following my attempt at instrumentation.

Case 4:—Mrs. M. Y. (J. H. H. No. 640887), 48 years of age and a short, stocky New Yorker, was sent to me in May of 1953 because she had had dysphagia for ten years, a difficulty which had made the patient withdraw from the company of her friends. Previously the lady had been sent to a roentgenologist who had made the diagnosis of cardiospasm. There was moderate dilatation of the gullet above a smooth constriction at the cardia (Fig. 5). I thought that the patient's story and films were typical of achalasia and I told her that esophagoscopy was hardly necessary and that as an office procedure simple stretching with the pneumatic dilator would probably give her an almost miraculous cure. The following day the patient's cardia was dilated before the fluoroscope without unusual difficulty. The pneumatic bag was properly placed and the stricture did not seem to be unusually tight. Directly after the dilatation the subject complained bitterly of pain in her left upper abdominal quadrant and around the scapula on that side. She felt faint and became pulseless but she did not lose consciousness. At my request, she drank a glass of water without difficulty. I was alarmed by the patient's degree and persistence of pain and I had her remain in my office. Three and a half hours after the dilatation her leucocyte count was 19,200, there was board-like rigidity in the left upper quadrant of her abdomen, and there was crepitation in the suprasternal notch;

it was perfectly certain from these signs that the esophagus had been torn in the dilatation of the cardia. The patient was hospitalized promptly.

In the hospital the patient was given nothing by mouth and all fluids were given intravenously. She was started on penicillin and on streptomycin parenterally. A film of her chest showed air in the mediastinal tissues but none under the diaphragm. While there was no temperature on admission, the rectal temperature rose to 101.6° the following day. Because the patient developed urticaria on her second day of hospitalization, her first antibiotics were stopped and she was given terramycin intramuscularly in doses of 800 mg. a day. This produced considerable local irritation so 0.5 gm. of that antibiotic was given intravenously twice daily.

On this therapy the patient's temperature fell satisfactorily and seven days after the therapeutic accident she was given, before the fluoroscope, a single swallow of Iodochloral (we would probably use Dionosil now) and it was seen to escape into the lower mediastinum from the lower end of the gullet (Fig. 6). You may imagine how "low" I felt, for I had thought that all was going quite well.

Because the patient was complaining so bitterly about the intravenous feedings, a Levin tube was passed into her stomach and she was given fluid and calories and terramycin through it. After five days of this the patient complained so much about the tube that it was withdrawn and a little barium was given orally for roentgen study of the lower esophagus. I was greatly relieved when it remained in the esophageal lumen; I could sleep peacefully once more. We gave a liquid and then a soft diet and oral doses of the antibiotic which had helped us so much. But a left-sided pleural effusion developed (or was detected) and this was aspirated. Fortunately it did not recur. Two weeks after admission the patient left the hospital without medication and with directions to take a soft diet for one week. She had no dysphagia.

Ten months after the dilatation and esophageal perforation the patient was in Baltimore and she stopped in to tell me that she had gained weight and had no subjective dysphagia. She ate meat and other things on a full diet and she could dine in public without embarrassment. She allowed me to examine her esophagus with the fluoroscope. I found it to be dilated and there was still some obstruction to the passage of barium at the cardia; the gullet had to be half full of fluid before it began to empty into the stomach. But that is not unusual when the functional result is excellent.

Case 5:—Mr. G. B. (M. G. H. No. 162691) was 70 years of age and a patient of the House Staff at one of the hospitals in Baltimore. He entered that institution June 19, 1954, because of asthma with chronic cough and dysuria. Lesser complaints were generalized weakness, lack of appetite, and constipation. Examinations showed a slightly low hematocrit and the changes of age, especially

in the electrocardiogram. But otherwise little of note was found until roentgen study of the stomach showed a small ulcer in the prepyloric region. On July 15th the patient was brought by the house officer to The Hopkins and to me, as an out-patient for a gastroscopic examination.

Mr. B. appeared weak when anesthetization of his throat was begun. He got on the table without much trouble, however, and he was a most cooperative patient. The Cameron gastroscope was passed easily and no ulceration could be seen in the stomach. A little red blood was noted in the gastric fundus and its source was not apparent; I presumed that it had come from trauma.

A review of the films which had been brought with the patient suggested the presence of a small hiatal hernia. With the feeling that the bleeding which we had seen and the borderline hematocrit might be produced by ulceration in a small thoracic stomach, esophagoscopy was performed. The constrictors of the pharynx were passed easily but the 'scope could not be gotten into the stomach, even with the use of the rubber obturator. The resistance was so marked at what I presumed to be the cardia that a biopsy was taken there; it was reported later to show normal esophageal mucosa. No lesion having been seen, the esophagoscope was withdrawn. Directly following the procedure and while still on the table the patient fainted, but he soon revived and he was taken to his hospital. I was a bit worried about him and in the late afternoon of the day of the endoscopy I inquired of the patient's house officer concerning our man. I learned that he had no temperature, that he was taking liquids, and that he seemed to be all right. Four days later our endoscopic nurse astounded me with the information that our patient's death notice was in the local paper.

I learned that on July 16th his rectal temperature had been 99° in the morning and 100.3° by the same route in the evening. A falling blood pressure was treated with a transfusion. No notes had been made about his ability to swallow that day and no perforation was suspected by the attending doctors. Nor had that been considered on the 17th when the patient's leucocytes were only 10,700; the patient had some pain in his chest and the diagnosis of early pneumonia had been entertained; antibiotics were started on that date. Also on the 17th the patient vomited a little blood; he received another transfusion and his temperature reached its highest point, 101.6° rectally. He died the following day in dyspneic fashion.

The house officers did not suspect the perforation of the lower esophagus which was found at necropsy and which was associated with a mediastinitis. Probably I would never have known of the sad termination of this case had it not been for the alert nurse.

All that I have said about the management of instrumental esophageal perforations has been by story telling. In that unscientific and indirect way I hope that I've brought out the first and, to my mind, the most important point

in the matter, viz., *prophylaxis through gentleness.* As one becomes more and more proficient in endoscopic procedures, he is quite likely to become a little lacking in the quality of gentleness when he performs them. May I suggest that you always pass esophageal instruments into the gullet not with fearfulness but with some awareness of your feelings when you first did that particular procedure? Thus your hand will be gentle and, if a perforation should occur, it is likely to be a small one. Secondly, realize that the hypopharynx and gullet of a 95 pound woman or of a frail oldster is not as resistant to trauma as that of a young man of average nutrition. Thirdly, pay attention to any post-instrumentational complaints which your patients may have and treat them *promptly.* Fourthly, let the initial treatment of perforations be hospitalization with, perhaps, when the perforation is a relatively high one, the Trendelenburg position (which I haven't yet tried), total intravenous or tube feeding with (and again I say perhaps, for I haven't yet used it) suction on the lower esophagus, and antibiotics. Lastly, don't forget the surgeon who may be of the greatest use if conservative measures are unavailing or if the injury to the gullet seems to be too gross a one for conservative treatment. Weisel and Raine[2], surgeons in Milwaukee, reported the prompt suturing of seven traumatic perforations of the esophagus over a period of two years "with no mortality and with minimal morbidity". You will know your surgeons and there are times when you'll deliberately choose a conservative one over a radical one—and vice versa. I am more inclined to favor early drainage of the neck than I am of the mediastinum, though the latter may become necessary, of course. Even if a few days of conservative treatment are decided on, it is often a comfort to have a surgeon behind one. And I've found the surgeons to be completely cooperative.

Probably esophagoscopic examinations are being made more frequently and esophageal treatments are being given by more persons than ever before. Therefore, there are probably more perforations occurring now than formerly. It is my belief that these accidents, which are inevitable, should be brought by us, rather than by the surgeons, into the light of day for discussion. That will do much to keep us careful workers and so redound to the benefit of our patients.

REFERENCES

1. Howard, J. T.: Adventures in the Esophagus. Southern M. J., **40**:197-206, (Aug.), 1947.
2. Weisel, W. and Raine, F.: Surgical Treatment of Traumatic Esophageal Perforation. Surg. Gynec. & Obst., **94**:337-346, (Mar.), 1952.

Discussion

Question:—My question is addressed to Dr. Howard. I realize there are other accidents to the esophagus than those made by the esophagoscope, and wonder why the paper was limited to those and did not include those made by the gastroscope. Also, where were the perforations?

Dr. Howard:—The question, as I understand it, is why I limited the talk to the esophageal perforations from esophagoscopy and esophageal instrumentation and did not include perforations with the gastroscope.

In the case which I hurried through, the last case that I reported, the patient had gastroscopy first without any trouble, presumably. Then we withdrew the gastroscope, reviewed the films, and we thought there might be some gastric tissue above the diaphragm, a roentgen effect on which the x-ray man had not commented. We put the esophagoscope down and we could not get into the stomach with it. We did not understand why, and the man died three or four days later; he had a perforation at the lower end of his esophagus. It was my impression that the esophagoscope had caused the perforation, though I could not have said for certain that the gastroscope had not done it. But we had visualized the interior of the stomach.

I have never had any trouble as far as perforations are concerned and to my knowledge—unless it was that case—with the gastroscope; so I had no cases of perforation with the gastroscope to report, though I realize that others have reported them, and that usually conservative measures, nonsurgical measures, have been adequate in those patients who have been perforated with the gastroscope.

It was from hospital gossip—and there is such a thing, I think you know—that I got the idea that there were quite a few esophageal perforations that weren't being talked about, that were hushed up. One of my friends, who is a roentgenologist, said, "You know I am a consultant for a number of hospitals and I am shown films of empyemas and of barium running out into the mediastinum following endoscopy. I don't hear anything about the patients afterward. What do you think about this?"

I said, "You know I have a guilty conscience. I have produced some of those perforations."

I think it is a good thing to talk about one's mistakes and to bring them into the light so that men who don't have the complication of perforation will continue to be careful, and men who have perforations will know that others are having trouble, too, and what's being done about them.

Dr. Victor Willner (New York, N. Y.):—I should like to ask Dr. Howard how he feels about the late perforations of the esophagus due to pressure necrosis particularly in heavy individuals with short necks or in those with marked hypertrophic arthritis of the cervical spine? It seems that due to prolonged pressure of the esophagoscope over the stretched mucosa overlying the hypertrophic or hyperextended cervical spine there is a production of local necrosis which will sometimes, on the 3rd, 4th or 5th day go to perforation. Those are the so-called late perforations as distinguished from the immediate perforations. How many of the late perforations did he have?

Another question is: Did he suspect a perforation?

Third question: Why did he prefer barium studies as the x-ray showed it instead of lipiodol which is a much safer procedure to use in suspected cases of esophageal perforations?

Dr. Howard:—The question, as I understand it, is: Do I think that later perforations might come from necrosis due to exostoses on the cervical spine, and also, why I use lipiodol or absorbable opaque substances rather than barium to x-ray these ruptured esophagi?

In answer to the first question, I know that it has been said that these hypertrophic joints in the cervical spine produce pressure which may make for perforations; they make bumps over which the esophagoscope and obturator have to go. I think that it is possible that these joints produce some obstruction and that trauma occurs when one goes "over the bumps". But, as far as I'm concerned, that's theoretical. I can't say that the man who had the somewhat late signs of perforation had such a spine; he was an elderly man, 66, and he could have had such a spine. But remember that his perforation was at the lower end of his gullet.

We use absorbable opaque materials for the patients to swallow when we suspect perforation because I think they probably do less harm to the tissues. Dionosil is the one I think we use, one which is very quickly absorbed and is used in roentgenography. You may remember, however, that in Case 4 we used barium and, fortunately, it did not run out into the tissues. Previously that patient had been given an absorbable radiopaque medium.

BLEEDING ESOPHAGEAL VARICES*

CHARLES B. RIPSTEIN, M.D.

New York, N. Y.

Of the collateral channels formed in cases of portal vein obstruction, the anastomoses in the submucosa of the lower esophagus present the most important clinical problem. Their tendency to severe hemorrhage is the cause of death in many patients with portal hypertension. In those individuals who survive the initial hemorrhage, repeated episodes of bleeding usually cause chronic invalidism.

Many attempts have been made to remove or obliterate these varices or to create new collateral channels to relieve portal hypertension. None has been wholly satisfactory.

Several factors operate in the production of hemorrhage from esophageal varices; and in any individual case, one or more may be predominant. They may be classified into three groups.

1. *Extravascular defects* are those factors which exert a mechanical effect on the varices or the overlying esophageal mucosa. In this group are included the effect of trauma due to passage of food, the effect of diaphragmatic movement, the changes produced by intrathoracic pressure, and finally, the effect of regurgitated gastric juice in causing peptic ulceration of the esophagus. These are localized factors which involve the esophagus alone.

2. *Vascular defects* are those abnormalities which are found in the vessel wall itself. Characteristically, esophageal varices are thin-walled, and the veins lie in the areolar submucosa and lack support.

3. *Intravascular defects* are those abnormalities which are present in the blood stream. Portal hypertension is the most prominent factor, but deficiencies in the clotting mechanism may also exist. Chronic congestion of the spleen causes increased destruction of platelets, and impaired liver function may lead to hypoprothrombinemia.

Most operations advocated for esophageal varices are designed to correct only one of these factors. In recent years, emphasis has been placed on the portacaval shunt[1] as a means of lowering hydrostatic pressure within the portal venous system. In our experience, this approach has not been satisfactory[2]. The majority of patients have received some immediate benefit in the regression of esophageal varices, but the improvement has been temporary. In only 7 of

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From the Department of Surgery, Albert Einstein College of Medicine of Yeshiva University and Maimonides Hospital, Brooklyn, N. Y.

30 patients followed for three or more years has there been lasting benefit, 23 have had recurrent bleeding or have died from hepatic failure. There is no doubt that portal hypertension is only one of the factors responsible for bleeding from esophageal varices, and massive hemorrhage has been reported with a normal portal pressure[3]. Furthermore, if increased portal pressure alone was responsible for massive bleeding from esophageal varices, one would expect such hemorrhages to occur with equal frequency in other areas of the gastrointestinal tract. Such is not the case. It would seem that the local factors involving the esophagus are the most important in producing the massive bleeding characteristic of esophageal varices.

This thought has occurred to many workers in the past. Baronofsky[4] has pointed out that there is an increased incidence of peptic ulceration produced by histamine-beeswax injection in dogs with portal hypertension. They considered that the acid-peptic factor was fully as important in causing bleeding from esophageal varices as the hydrostatic pressure in the portal system. They demonstrated that a 90 per cent gastric resection did offer some protection in a small group of patients.

Other attempts have been made to correct the local factors by periesophageal venous stripping, by mediastinal packing to create adhesions, and by excision of the lower esophagus. None of these methods has given consistently good results in long-term follow-up. We have been impressed by the frequency of peptic esophagitis or esophageal ulceration associated with varices in fatal cases. In the past five years, at this hospital, 22 patients have come to autopsy following death from bleeding esophageal varices. In 10 of these, careful examination has revealed evidence of gross or microscopic esophageal mucosal ulceration.

Because of these findings, we have felt that no single procedure could be effective in all cases of esophageal varices, but that it is necessary to adapt the operation to the individual and to correct as many factors as possible.

The differential diagnosis of hematemesis may be extremely difficult. The establishment of a diagnosis of hepatic cirrhosis is of some help but does not prove that the bleeding is from esophageal varices. Peptic ulceration of the stomach and duodenum is common in cirrhotics, and these lesions may bleed. Emergency liver function tests, such as the thymol turbidity or B.S.P. retention, are not completely reliable in the presence of massive hemorrhage and shock. The best diagnostic criteria in our experience have been a careful history and the previous demonstrating of esophageal varices by barium swallow or esophagoscopic examination.

The emergency treatment of choice has been balloon tamponade, with the use of a topical gelfoam-thrombin mixture. Transesophageal ligation has been avoided because of the fact that in our autopsied cases, bleeding points have

been visualized as high as the arch of the aorta and it would require a formidable procedure to control bleeding by surgical means.

Because of our disappointment with the long-term results of portacaval shunts, and because of the high incidence of peptic ulceration of the overlying esophageal mucosa, we have adopted the following plan of attack in patients with recurrent bleeding from varices.

Through a left thoracoabdominal incision, the lower esophagus, stomach, spleen, and left kidney are visualized. The lower esophagus is stripped, ligating and dividing all venous channels and performing a bilateral vagectomy. The left phrenic nerve is divided to immobilize the diaphragm. A 90 per cent subtotal gastric resection is carried out; the spleen is removed; and if the splenic vein pressure is over 300 millimeters of water, a spleno-renal end-to-side anastomosis is carried out.

This procedure has the following effects:

1. Portal pressure is lowered, and the portal vascular bed decreased.
2. Gastric acidity is abolished.
3. The factor of hyperopleonasm is removed.
4. Diaphragmatic movement is eliminated.
5. The periesophageal venous channels are interrupted, and mediastinal adhesions are created.

This procedure has been carried out in 6 patients who have been observed over a period of at least two years. None have had recurrent bleeding, although one has subsequently died of hepatic failure. It would appear rational to attempt correction of many of the factors causing bleeding from esophageal varices rather than to focus attention on portal hypertension as the sole important lesion.

REFERENCES

1. Blakemore, A. H.: Portacaval Shunting for Portal Hypertension. Surg. Gynec. & Obst. **94**:443, 1952.
2. Ripstein, C. B.: Experiences with Portacaval Anastomosis in the Treatment of Portal Hypertension. Surgery **34**:570, 1953.
3. Rack, F. J., Mincks, J. A. and Simeone, F. A.: Observations on Etiology of Esophageal Varices. Arch. Surg. **65**:422, 1952.
4. Baronofsky, I. D.: Portal Hypertension. Surgery **25**:135, 1949.

SOME PRACTICAL CONSIDERATIONS OF MASSIVE GASTROINTESTINAL HEMORRHAGE*

C. REID EDWARDS, M.D.

Baltimore, Md.

When asked to present a paper, I decided on this title because I do not know of any place I would prefer to start a discussion than before a group of medical students or of internists, laboratory men, and surgeons, who might be involved in this very important problem.

You know no group of cases admitted to our hospitals gives us more concern than the patients who are bleeding into the alimentary tract, and, in order to crystallize our thinking about it at the moment, I decided to limit this discussion to the cases of massive gastrointestinal hemorrhage. This data has been collected from 155 cases admitted to the hospital with a complaint of bleeding from the alimentary tract, or they came because they felt weak and exhausted, or were in shock.

Many of our patients at the University Hospital come to us through the emergency department, and are first seen by the house men, and, as a compliment to the house men in most hospitals, I think more energetic treatment is initiated in that type of patient than one that might be referred from doctor's office to doctor's office.

Of the 155 cases, 108 were classified as cases of massive hemorrhage. This poses a problem for any group of clinicians. Of these 108, or 69.6 per cent of the total, 34 had a history of previous bouts of bleeding, so that immediately in this group we get patients who have had bleeding episodes before, and that should give us a very good line on the patient immediately he is admitted, as to the etiology of his hemorrhage. We have excluded from this group all of the patients who are routine long-standing duodenal ulcers or gastric ulcers, with very moderate amounts of bleeding; who come in because of the symptoms of ulcer rather than symptoms of hemorrhage, as these patients; can proceed through a very regular method of evaluation, but in the patient with massive hemorrhage, the circumstances are not quite the same.

Why do we define this group of massive hemorrhage cases as against those of just minor bleeding? Because immediately they are placed in the category of patients so dangerously ill that whatever we do must be done very expeditiously.

During the course of now over forty years that I have been doing abdominal surgery, I have watched these massive bleeding cases, as many of you have,

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I am sure, and any clinician is challenged to the very limit of diagnostic ability as well as his method of applying the proper therapy. Therefore it is imperative that we do whatever we can do to make the diagnosis as quickly as possible. So, therefore, we like to define the group and divide it as one of minor hemorrhage, and one of massive hemorrhage, and in the latter, we begin the immediate evaluation.

Why do we define them as massive hemorrhage? Well, one of three things or a combination of any of the three usually exists. First is shock. A patient with a massive hemorrhage is in shock, usually when the first doctor sees him. He is in shock when he comes into the emergency room. He is in shock when he is transported to a hospital. Usually there is, and in our criteria we expect there to be, a hemoglobin of 60 per cent or less. Then, if the patient is in shock, and there is evidence of gastrointestinal bleeding, someone usually starts a transfusion as quickly as the patient's blood can be typed and matched and if, after the administration of two pints of blood, the patient's condition has not been restored, or he shows evidence of not responding, he certainly should be defined as a case of massive hemorrhage.

In the event that we do immediately classify a patient with massive hemorrhage, what should we do? In the first place, since 34 of this group of massive hemorrhage have a history of previous bleeding bouts, we are most likely dealing with patients with peptic ulcers, because they provide the greatest number in this group, or we may be dealing with patients with esophageal varices incident to liver cirrhosis. Therefore, if the patient has vomited blood, as one of the first evidences of his hemorrhage, we want an esophagoscopic examination made at once. That is difficult to obtain, especially late at night, but, if possible, we would like to have this examination made. While in our experience it has not been a common etiological factor, it has been observed often enough to justify a procedure which we think is worthwhile.

If the doctor making this examination finds bleeding varices, a balloon of some type can be introduced immediately. This probably may arrest the massive flow of blood, and make it possible to transfuse him up to a safe state, and proceed with an operation which is indicated, instead of permitting that patient to go from day to day getting quarts and quarts of blood and winding up a few days later maybe having 25 or 30 transfusions, and reduced to the lowest ebb of life. If he has to undergo a major operation, he is not adequately prepared to defend himself.

If no bleeding is encountered in the esophagus, we ask for a gastroscopic examination. If he has a massive hemorrhage from the stomach, the gastroscopist will not be able to identify it, but he will at least be able to say there is very active arterial bleeding from the stomach, which is sufficient to indicate an immediate operative procedure.

If the bleeding is from the pylorus down, it is usually the case that he will not vomit blood, but I, of course, know fully well that they do vomit from a bleeding duodenal ulcer on occasion, when the blood is regurgitated in quantities into the stomach.

If there is a history of previously existing ulcer and previous bleeding bouts, we believe that that is sufficient indication to warrant operative procedure; however, if there is no history of an ulcer, yet bleeding is quite likely from below the stomach, we request an immediate x-ray examination.

Like many of you in the audience, I was against this for many years, but I am firmly convinced by experience in our clinic that it is a perfectly safe procedure. It has made possible the diagnosis of an ulcer in a number of cases, and we have had absolutely no bad results from this procedure.

If the patient has evidence of an impending perforation, has upper right quadrant pain and rigidity, marked tenderness, then we would not ask for an x-ray examination; in fact, we would prevent it, but that is totally up to the judgment of the physician.

What is the etiology of these bleeding cases? Thirty-nine of our cases were proven to be duodenal ulcer, and 19 gastric ulcer; therefore, you have a total of 58 out of the 155 that were peptic ulcers. There were only nine esophageal varices, two marginal ulcers, and the amazing thing, that only one carcinoma of the stomach was responsible for a massive hemorrhage. That goes along very well with our experience that most of our patients who have carcinoma of the stomach, come in anemic, but not as a result of massive hemorrhage. It was rather surprising that we had but one out of this group that had a massive hemorrhage from a carcinoma of the stomach. That is another argument that we should not postpone the gastric carcinoma waiting for bleeding to occur.

There were three cases of gastritis, three of blood dyscrasias, two of duodenal diverticula, and 49 of undetermined origin. The rest of them are scattered over a group of pathological entities, usually averaging about one each.

The group of cases of undetermined origin—this sounds like a very large percentage in this total of 155, and that is because it represents not only cases which were thoroughly worked-up, but also it represents quite a few who signed themselves out of the hospital before the total examination could be completed, and in the cases of undetermined origin, we have, of course, probably a few cases of blood dyscrasia which have not been proved. It has been our experience over the years that this is the hardest group in which to make a real contribution from the diagnostic standpoint.

Whose responsibility is it to take care of these patients? It has not been many years since our medical services were not very much interested in the

early operation. I am sorry to report that that was the attitude of many surgeons throughout the country, but over a period of years both have been won, in our hospital especially, to an early consideration. Now, while most of our service cases are admitted to the medical service, if there is a massive hemorrhage, the surgical department is alerted before the patient has had the second pint of blood, and, from that time on, the conduct of the case is one of mutual responsibility. The laboratory, of course, comes into this, too.

Now we are trying to maintain an attitude towards these patients as follows: If two pints of blood have not made the patient very much better, possibly they have restored his volume of blood in cases that haven't bled too much, but if, at the end of two pints of blood, the patient does not show clinical evidence of marked improvement, we immediately prepare that patient for surgery, and it has resulted in an early operation in a great many patients.

I am always terribly concerned when I am called to operate on a massive hemorrhage case when he is getting his 15th or 22nd pint of blood. While blood is the greatest means of saving the lives of these people, we know perfectly well that the patient who is of the age group where most likely liver damage and kidney damage have already been observed, it doesn't take very much more of an insult, whether it is chemical, biological, the anesthetic or the operation, or a combination of them all. Certainly morbidity and mortality have been reduced in a large group of patients since we have been insisting on earlier operative procedures.

The danger of delay in all of these patients, of course, is one where the hepatorenal syndrome is so likely to be encountered. No matter what figures you read, what articles you study, you realize that a liver that is already somewhat damaged is not going to be able to endure very much more. Therefore, I think that the responsibility of handling these cases is mutually shared by the internist, the laboratory department, and the surgeon. I can't see any place for the psychiatrist in this group.

My experience has been that if a good doctor, a good general practitioner, or a good internist, cannot handle a peptic ulcer patient satisfactorily, then the psychiatrist has to be called in to do it, and the patient is not being treated for peptic ulcer but for a psychiatric indisposition.

Certainly we teach that the routine indication for operation for peptic ulcer is perforation, hemorrhage (whether it is recurring or massive), obstruction, and intractable pain.

Since such a high percentage of our patients with massive hemorrhage have the history of long-standing ulcers, then why shouldn't we get busy very much earlier and rescue a number of them from a long, serious illness, and restore them to perfect health?

Discussion

Dr. Donald C. Collins (Hollywood, Calif.):—Have you had any experience with the use of powered gel foam plus thrombin in a milk mixture reported so successfully from the Receiving Hospital in Detroit, in the handling of massive and duodenal hemorrhages?

Dr. Edwards:—Yes, Doctor. We have had brief experience in a few of these cases and it has been very satisfactory. The exact number I cannot recall, and certainly it has been observed in two or three cases where there has been temporary benefit during which time the patients could be better stabilized and then carried on from there.

Dr. F. H. Voss (Phoenicia, N. Y.):—Do you agree with the amount of blood necessary to produce this so-called classified massive hemorrhage?

Dr. Edwards:—Yes, we have arbitrarily fixed two pints as the starting point. Of course, a number of those patients, after they get the third pint, will be very much improved, and then they get the fourth, but if, at the end of the two pints, we are still concerned, surgery is alerted so they will be ready to go ahead with it in case the patient does not show tremendous evidence of improvement.

I think the reference to the blood quality and quantity is important, because blood volume studies certainly are of very great importance, and now, since we have radioactive substances with which these studies can be made more accurately, we are learning a lot about it, and I think we are going to be able to classify our patients a bit better.

Dr. Richard Bachmann (Springfield, Mass.):—As pointed out, in a large percentage of cases the origin of the bleeding was not established. It may not be necessary to do an examination in that case. Would you go ahead and do your surgery without waiting to establish a definite diagnosis?

Dr. Edwards:—I tried to indicate, Doctor, that by esophagoscopic, gastroscopic, and x-ray examinations we would have a positive origin of the hemorrhage, if possible. I am aware that throughout the country today a number of surgeons have reported gastric resection without evidence of ulceration. I am not in favor of that. Of course, we all have to do it occasionally, but very infrequently.

I like the pathologist to check on the material I have sent to him, and I want to send something which is positive. I realize a number of cases are reported throughout the country, and in our clinic we are guilty of about three of them, in the last four years, in which the patients had histories suggestive of peptic ulcer, but no peptic ulcer could be demonstrated. A subtotal resection was done and the patients have been cured. I realize that a surgeon should sort of hang his head in shame when he does that sort of job, but, after all, if

the patient gets well, it is a good contribution but certainly not a good thing to be recommended as a universal procedure.

Dr. Richard I. Kilstein (New York, N. Y.):—Speaking about criteria, when the patient is in continual shock, and you are pouring in blood at the rate of 2,000 c.c. per day, when does the surgeon feel that he can go into that abdomen without having a mortality on his hands?

Dr. Edwards:—I think both of us might take a crack at that. That is a good question. Doctor, my experience has been, of course, I am sure, that of many surgeons, that occasionally you encounter a case like that, and you have to decide right then whether you are going to make a rather minor surgical attempt to control bleeding, or let the patient die without surgical intervention. In other cases, where the hemoglobin is down, blood pressure is down, I have advocated opening the abdomen under local, exposing the duodenum, from which this hemorrhage is usually occurring, transfixing the bleeding vessel, and then getting out.

You are not operating there to cure a patient of a peptic ulcer. You are operating to rescue him from a fatality due to a hemorrhage, and under those circumstances we have had a few cases recover.

Dr. Kilstein:—I want to ask, before you leave that last statement, what your percentage of recovery is in those cases?

Dr. Edwards:—The worst case I can recite is that of a man who went on the table with a hemoglobin of 26. Obviously, he was bleeding to death. He had had something like five quarts of blood during the night, when I saw him on a Sunday morning, with another surgeon, I said, "I don't think you have anything to lose by operating on this man. You may gain something."

He was never x-rayed. His abdomen was opened. The ulcer could not be palpated. The stomach was opened, and when the mucous membrane was elevated, there was a little column of blood shooting about four inches in the air, about the size of the lead in a pencil. It was transfixed, and transfusions were continued, and he recovered.

I have seen that happen several times, but it is not a thing any man wants to do or recommend. It is done in desperation, when you have to decide between sure death and a very slight possibility of life.

MEDICAL MANAGEMENT FOR GASTRIC ULCER*

SIDNEY M. FIERST, M.D., F.A.C.G.
JAMES B. GABRIEL, M.D.
and
ABRAHAM WERNER, M.D.
Brooklyn, N. Y.

A sharp disagreement persists between the advocates of medical or surgical therapy in the management of gastric ulcer. The statement is frequently made[1-4] that up to 10 per cent of supposedly benign gastric ulcers are really malignant and, therefore, that the therapy of gastric ulcer should be regarded primarily as a problem for the surgeon. This has led, in many instances, to the unrestricted surgical treatment of this entity. The disabling postgastrectomy sequelae, including the dumping syndrome, nutritional deficiency, hypochromic anemia, and inability to gain weight, which occur in 5 to 10 per cent of patients after resection, dictate the need for discretion in assigning patients with gastric ulcer

TABLE I

AGE DISTRIBUTION OF PATIENTS

Age (Years)	Number of Patients
21-30	1
31-40	13
41-50	26
51-60	20
61-70	8
71-80	2

to surgery. In this regard, pleas for individualization in the choice of either medical or surgical therapy have been voiced recently[5-8].

Statistics alone are dangerous guides to therapy. The gastroenterologist and internist must make a careful effort to evaluate each patient individually and only then to arrive at a decision regarding the type of therapy indicated. The present study was undertaken to determine the results in a series of patients with gastric ulcers in whom clinical judgment presaged benignity and for whom medical treatment was accordingly instituted.

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From the Medical Department, Maimonides Hospital, Brooklyn Veterans Administration Hospital and Department of Internal Medicine, State University of New York Medical College at New York City.

This preliminary report is based on personal observations on the course of gastric ulcer in a small group of 70 patients followed for between 2 and 8 years. There were 48 men and 22 women ranging in age from 26 to 76 years, with the greatest incidence occurring in the fifth and sixth decades (Table I). The duration of symptoms ranged from 4 weeks to 14 years. In 4 instances the diagnosis of gastric ulcer had been made 8, 5, 2 and 1 years before the patients came under our observation.

Weight loss was a prominent presenting symptom (Table II). Twenty-eight patients had lost between 10 and 20 pounds and 21 patients less than 10 pounds. Only 20 had not suffered significant weight loss.

Gastric analyses after histamine (Table III) tended to show a low acid level. In one patient with a fundic ulcer, anacidity was present even after four histamine tests. Because of this fact and the chronicity of the ulceration in the fundus, total gastrectomy was performed, only to reveal a benign ulcer. In 29 patients hypoacidity with free acid values below 20 existed, and in 20

TABLE II

WEIGHT LOSS

Degree	Number of Patients
None	20
Less than 10 pounds	21
Less than 20 pounds	28
More than 20 pounds	1

patients normal acidity values were present. Only 20 patients had values above 50 units.

The ulcerations occurred predominantly in the lower two-thirds of the stomach (Table IV). Only 6 occurred in the cardia and fundus, 24 in the body and 22 in the antrum and pylorus. Seventeen patients had lesser curvature ulcerations. One patient, in whom a benign ulcer of the greater curvature was diagnosed gastroscopically, refused surgery at first. Two years later, with recurrence of the greater curvature ulceration, surgery was insisted upon because of the high incidence of malignancy associated with ulcers of the greater curvature. He was found to have multiple benign ulcerations.

The accuracy of diagnosis is an important factor in determining the type of therapy to be used. All patients in this series underwent gastroscopy at least once. In six patients with prepyloric lesions, in three with posterior wall lesions and in one each with the lesion in the cardia or fundus–a total of 11–the ulcers could not be visualized even though they were apparent on x-ray. In four patients, lesions not visualized on x-ray were seen by means of the gastro-

scope—twice on the posterior wall, once in the cardia with the patient in the erect position and once in the antrum at the angulus.

The lesions visualized by gastroscopy were correctly diagnosed on direct examination in 91 per cent of instances. The overall accuracy was increased to 96.6 per cent if the procedure was repeated in doubtful cases after a trial of medical therapy. The diagnostic reliability of the x-ray was inferior to that of gastroscopy for those ulcers which were visualized by each method. A higher percentage of 94.3 per cent of the lesions, however, was visualized by x-ray. Accordingly, the overall accuracy of the x-ray was greater than that of gastroscopy in the diagnosis of gastric ulcers. The tendency to mistaken diagnoses in both x-ray and gastroscopy was in the direction of calling benign ulcers malignant. In only one instance was a malignant ulcer called benign gastroscopically. In one instance a malignant ulcer called benign by x-ray was later correctly diagnosed to be malignant gastroscopically.

Of the 70 patients, 30 underwent surgery. Twenty-two were sent to gastrectomy because of intractable, recurrent pain and nonhealing of the ulcer.

TABLE III

GASTRIC ANALYSIS FOR FREE ACID (Histamine .1/10 Kilo.)

Units Free HCl	Number of Patients
0	1
Less than 20	29
20-50	20
More than 50	20

The subsequent follow-up in these patients has shown 18 to be completely symptom free. Two have postgastrectomy syndrome. One has developed macrocytic anemia and is a nutritional problem four and one-half years after total gastrectomy for an ulcer at the fundus. One patient developed carcinoma in the residual gastric stump three years after surgery and died.

Four other patients had gastrectomy for hemorrhage. One patient had recurrent annual attacks of gastric ulceration for four years before a massive hemorrhage forced her to acquiesce to surgery. She is doing well one year later. One patient, whose ulcer could not be visualized adequately, developed, after gastroscopy, pneumoperitoneum without evidence of perforation. The ulcer was thought to be benign at the time of exploratory laparotomy. Massive hemorrhage occurring 6 weeks later necessitated subtotal gastrectomy. Carcinoma *in situ* was found. He died 3 years later of an independent carcinoma of the body of the pancreas. The other two patients had surgery 2 and 5 years after the initial diagnosis of gastric ulcer.

Three patients were sent to operation because of recurrent ulceration occurring within one year. Multiple ulcerations of the lesser curvature and in

the antrum were present in one of these. The recurrence of ulceration within the first year was taken as an index of intractability, since the ulcer recurred despite medical management. In one patient an associated duodenal ulcer caused pyloric stenosis. In no instance in this series was gastric ulcer responsible for pyloric obstruction. One patient developed recurrence of gastric ulcer with acute perforation 18 months after his first attack.

Thus, in this group of 70 patients, clinically diagnosed as having gastric ulcer, three cases of gastric carcinoma were uncovered, two of which were carcinoma *in situ*.

Forty patients were treated medically. In this group the recurrence rate of gastric ulcer was high (Table VI). In the first five years almost one-half of these patients suffered recurrence of a gastric ulceration. The location of the ulcer was, in most instances, near the site of the original ulcer, but in one-third of the cases was at a different site.

TABLE IV

LOCATION OF ULCER

Fundus	4	
Cardia	2	
Body	24	Anterior wall 14 Posterior wall 10
Antrum	12	
Prepylorus	10	
Lesser Curvature	17	
Greater Curvature	1	

Of the patients who did not develop a recurrence 50 per cent had attacks of abdominal distress, nausea and vomiting severe enough to require medical attention. Thus only 10 patients of the 40 treated medically have been completely well for 3 or more years.

COMMENT

The problem of distinguishing between benignity and malignancy in gastric ulcer is one whose solution should lie safely within the grasp of the trained and careful physician. A small number of early cases of carcinoma will be missed, but the cure to have been expected after gastrectomy in these cases can be balanced off against the operative mortality which would accompany a less discriminating surgical approach to the problem. For example, taking the figure that 10 per cent of gastric ulcers are malignant, that surgery will cure 40 per cent of these, and that the mortality rate of gastric resection is about 2 per cent, the survival rate for a group of gastric ulcer patients treated surgically would be 92 per cent. The survival rate of a similar group receiving

no treatment would be 90 per cent, a mortality difference of only two per cent. From this there can be seen the wisdom and desirability inherent in a method employing careful search for malignancy in individual patients with gastric ulcers as the basis for surgical intervention.

Brown[9] has shown that carcinoma develops in ulcer in only 1.1 per cent of cases. In our small series only two cases of cancer *in situ* were noted—an incidence of 2.8 per cent. Thus the fear of carcinoma should be replaced by criteria of intractability.

This attitude, of course, presupposes knowledge and care in diagnosis. Adequate and skillful fluoroscopy after complete dark adaptation is important in order to note localized rigidity and diminished peristalsis. Mucosal and

TABLE V

DIAGNOSTIC ACCURACY OF GASTROSCOPY AND X-RAY

	Gastroscopy 70 Cases	X-ray 70 Cases
Ulcers Visualized	59 (84.3%)	66 (94.3%)
Ulcers not Visualized	11 (15.7%)	4 (5.7%)
Correct Diagnosis Initial Examination	54 77.1% (of total) 91% (of those visualized)	60 85.7% (of total) 90.9% (of those visualized)
Correct Diagnosis After Repeat	57 81.4% (of total) 96.6% (of those visualized)	62 88.5% (of total) 93.9% (of those visualized)
Errors	Malignant called Benign 1	Malignant Called Benign 2
	Benign called Malignant 4	Benign called Malignant 4

double contrast air technics should be utilized. Spot films with varying degrees of pressure are valuable.

Gastroscopy is an important adjunct to x-ray in improving diagnostic accuracy. The benign ulcer is a sharply margined crater with a gray-white, clean base. There is no evidence of rigidity, nodularity or irregularity although increased tone locally as the result of an associated inflammation may give it a certain rigidity. It is for this reason that a benign ulcer which is chronic and indurated may be mistaken for a malignant one. The gastric rugae, however, are effaced by air insufflation, unlike those in malignant infiltration. The healing benign ulcer also has a characteristic pink rim of granulation tissue. Observed in the path of peristalsis the ulcer may float first on the crest and then it may disappear temporarily into the trough of the wave.

A carcinomatous ulcer, on the other hand, exhibits a necrotic base of many colors. The overhanging margins are frequently steep and craggy. They are

rigid, nodular and irregular, and the adjacent mucosa will not flatten out with air inflation.

The gastroscope, therefore, is a valuable instrument if the lesion is visualized. The colors of living tissue created by variations in blood supply and tissue thickness help the trained eye to the correct diagnosis, especially after repeat examinations.

The question may well be asked, "Is medical therapy of gastric ulcer worthwhile?" Thirty of these 70 patients had to undergo surgery for various

TABLE VI

NATURAL HISTORY GASTRIC ULCER, 70 PATIENTS

Referred to Surgery 30–		Postoperative Follow-up	
Intractability	22	Well	18
Pain			
Nonhealing		Postgastrectomy syndrome	2
		Macrocytic anemia	1
		Carcinoma in stump	1
Hemorrhage	4	Well	3
(Assoc. Duod. Ulcer 1)		Died Ca Pancreas	1
Recurrence	3	Well	2
(Assoc. Duod. Ulcer 1)			
Obstructing		Postgastrectomy syndrome	1
Perforation	1	Well	1
Medical Therapy Total 40–		No Ulcer Visualized–	
Recurrences	20	Attacks of discomfort, epigastric distress,	
One year	4	nausea or vomiting,	
Two years	2	tenderness	10
Three years	7	Well–10	
Four years	4	Three years	4
Five years	2	Five years	3
Eight years	1	Six years	2
		Seven years	1

complications. Nonhealing and persistence of the niche indicated either penetration or nutritional and vascular factors perpetuating the ulceration. Hemorrhage was another indication for terminating medical therapy. It is interesting to note that cancer of the stump occurred after resection of a benign ulcer in one patient.

In the 40 cases treated medically, only 10 have remained completely well. Recurrences of ulceration have occurred in 20 patients with good response to an adequate medical regimen being the rule. In the remaining 10 cases, no evidence of ulceration has appeared, although mild symptoms of dyspepsia have occurred from time to time. Thus, one-half of the group of patients treated

medically have experienced recurrence of gastric ulcer. The remaining half have progressed satisfactorily without surgery.

Summary

1. A series of 70 patients with gastric ulcer were followed from 2 to 8 years.

2. Thirty patients had to have surgical intervention for complications of ulcer.

3. Forty patients were treated medically. Twenty developed recurrences of ulceration which responded to further treatment. Ten patients had recurrent attacks of pain and abdominal distress which responded to intensive medical management. Ten patients have remained completely well.

4. Carcinoma was not a major problem in differential diagnosis. With careful progress check-ups the accuracy of x-ray diagnosis was 94 per cent and of gastroscopy 96.6 per cent of the lesions visualized.

5. The error most frequently made was in calling benign ulcer malignant, rather than malignant ulcer benign.

REFERENCES

1. Ravdin, I. S. and Horn, R. C., Jr.: Gastric Ulcer and Gastric Cancer, Ann. Surg. **137**:904, 1953.
2. Allen, A. W. and Welch, C. E.: Gastric Ulcer. The Significance of this Diagnosis and its Relationship to Cancer, Ann. Surg. **114**:498, 1941.
3. Lahey, F. H.: Diagnosis and Treatment of Peptic Ulcer, Post-Graduate M. J. **3**:342-352, 1948.
4. Ochsner, A. and Blalock, J.: Carcinoma of the Stomach; Necessity for Re-evaluation of Therapeutic Philosophy, J.A.M.A. **151**:1377, 1953.
5. Smith, F. H., Bales, R. S. and Jordan, S. M.: Problem of the Gastric Ulcer Reviewed, J.A.M.A. **153**:1505, 1953.
6. Gott J. R., Shapiro, D. and Kelty, K. C.: Gastric Ulcer, A Study of 138 Patients, New England J. Med. **250**:499, 1954.
7. Browne, D. C., Mitchell, R. E., McHardy, G. and Welch, G. E.: Evaluation of Surgical Intervention in Gastric Ulcers, J.A.M.A. **155**:807, 1954.
8. Brown, H.: Benign Ulcer and Carcinoma of the Stomach, J. Am. Geriatric Society **1**:177, 1953.
9. Flood, C. A. and Hennig, G. C.: Recurrence in Gastric Ulcer under Medical Management, Gastroenterology **16**:57, 1950.

HEADACHES ASSOCIATED WITH GASTROINTESTINAL DISTURBANCES*

ZACHARIAH R. MORGAN, M.D., F.A.C.G.

Baltimore, Md.

While there is a voluminous literature on headache, there has been a paucity of papers concerning its relationship to the gastrointestinal tract. It is not intended here to cover such a vast field, but an attempt is made to point out the many conditions which are associated with headache and which should be considered by the gastroenterologist. Since at times the gastrointestinal symptoms precede the headache, it should be emphasized that the onset of the patient's condition may be with digestive complaints and therefore the gastroenterologist is the first to see the case. The most frequent gastrointestinal symptoms accompanying headache, are abdominal distress, pain, nausea, vomiting, anorexia, epigastric fullness, pyrosis, constipation and diarrhea.

We are indebted to Ray and Wolfe[1] for the monumental investigation in the pathologic anatomy and physiology of headache, and no understanding of headache is possible without some knowledge of the pain sensitive structures of the head and the disturbances which bring about their stimulation. Migraine is one of the oldest conditions known to mankind. It is described as an intermittent occurrence of headache, usually unilateral, preceded by auras, accompanied by nausea and vomiting, and often associated with scintillating scotomata and occasionally by temporary partial blindness and later followed by exhaustion. The classical symptomatology presents no problem in diagnosis, but at times there is a marked variation in the symptoms and the degree of headache.

Brahms[2] described a clinical picture of cranial migraine associated with severe abdominal pain. He was among the first to direct attention to the possible connection between head pain and abdominal pain of periodic nature, and pointed out that abdominal migraine may manifest itself in three forms: 1. The ordinary type, in which the epigastralgia occurs with or without the headache. 2. The vicarious type, in which the migraine headache exists alone for a time; and later the abdominal symptoms appear as the only manifestation. 3. The larval or irregular type, in which the periodic attacks consist of vomiting, etc., while the epigastralgia is less marked.

Abdominal migraine has not received much attention in the literature. While it is a comparatively rare condition, insufficient emphasis has been given to this condition. Most of the textbooks on gastroenterology either do not mention this condition at all or in such a minor way that it is overlooked by the average reader. There is an occasional report in the literature of cases

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which have had one or more futile abdominal operations which might have been avoided had the internist or surgeon thought of this diagnosis as a possibility in those cases which have the association of the usual manifestations of migraine with severe abdominal pain. Kleckner and Horton[3] compared the incidence of the concurrence of peptic ulcer and migraine, and report that it is far below the incidence of peptic ulcer in the general population.

In a series of the 32 cases of migraine, Blitzstein and Brahms[4] found that abdominal pain was the outstanding symptom in the clinical picture, occurring in periodic attacks similar to the attacks of hemicrania in the ordinary form of migraine. They pointed out that the outstanding features of the condition described are periodic attacks of severe abdominal pain, with normal intervals, in a person who has a personal or family history of typical migraine. The attacks resemble very closely the ordinary attacks of migrainous hemicrania, except that abdominal pain occurs instead of headache. The fact that four of their patients were operated on and nothing was found to explain the attacks strengthens the belief that these were cases of atypical migraine. Piper[5] reports a case of a 16-year old girl who had several attacks of abdominal migraine with the cyclical vomiting of childhood and believes that there is a great similarity of these conditions. Brain[6] and Holt and Howland[7] state that the cyclical vomiting of childhood is often followed by migraine in later life. Groh and Veal[8] report a case of abdominal migraine and discuss in detail the many possible causes of the severe abdominal pain associated with this condition.

Friedenwald and Feldman[9] described a characteristic headache and migrainous attacks associated with intermittent duodenal stasis. Cunha and Day[10] in describing the symptoms of duodenal stasis caused by an aberrant superior mesenteric vessel mention headache, dizziness and vertigo which they think may be due to the absorption of toxic products through the duodenal wall. This has been called "duodenal migraine".

Buchanan[11] reported seven cases of abdominal pain as a part of the migraine syndrome, stating that attacks of abdominal pain as a radical of the manifestations of the migraine characteristic are exceedingly rare. In reviewing his cases, however, he feels that the percentage of patients on whom operations have been performed was sufficiently large to suggest that the necessary emphasis has not been placed on the futility of operating upon or administering medication for this condition.

Moore[12] is very critical of the term abdominal migraine, stating that the abdominal symptoms are due to discharges arising in cortical areas 6, 5 and 3 of Brodman or in the diencephalon which causes abnormal motility of the intestinal tract with resultant pain and discomfort. He believes that the term abdominal migraine should be discarded and abdominal epilepsy substituted, and suggests that anticonvulsant drugs should be used in its treatment.

Headache Due to Gastrointestinal Allergy

For many years there has been a controversy regarding allergy of the gastrointestinal tract as an etiological factor of migraine headache. Some authorities believe that migraine attacks associated with vomiting are the result of an allergic process. There are numerous reports of severe headache with various abdominal symptoms which have been successfully relieved by allergic therapy through avoiding certain foods in the patient's diet. Vaughan[13] is usually given credit for the first description of the relationship of allergy to migraine when he obtained relief by excluding the offending foods from the diet and the return of symptoms by again feeding these foods. Rowe's[14] elimination diets are a great help in establishing the offending foods. Skin tests are of little value in the diagnosis. Thomas and Johnston[15] presented several case histories of allergy causing severe headache with gastrointestinal manifestations, which were relieved by the treatment usually outlined by allergists. Friedenwald and Morrison[16] described a case where elimination diets revealed that milk foods together with fish were responsible for migraine headaches associated with nausea and vomiting. Exclusion of these foods cured the patient, and recurred only when the diet was not followed.

The type of pain described by allergists is usually not the sharp cutting or burning type of pain, but is rather dull and cramping in character. A very common form of gastrointestinal allergy accompanied by severe headache is abdominal colic which may simulate gallbladder disease, peptic ulcer or even intestinal obstruction. A careful history will often reveal that the attacks occur after eating certain foods. The attacks often date from childhood and are associated with other types of allergy such as hay fever, urticaria, etc. There is usually a history of allergic manifestations in other members of the family. Often there is a rise of leucocytes with eosinophilia. Seigal[17] reported five cases, all members of one family. Paviot and Chevallier[18] reported the occurrence of hemorrhage, erosions and edema of the gastric mucosa associated at times with severe headache. Bauer[19] called attention to an allergic peritonitis, characterized by paroxysmal attacks of intense colicky pain, distention, ridgidity, fever and leucocytes coexisting with marked headache. Finally we must bear in mind the possibility of an allergic basis in cases of all illnesses with headache in conjunction with acute abdominal pain, vomiting and diarrhea. Hemorrhages also have been described stemming from allergic stomach disease. Many patients seeking medical aid are convinced that constipation, overeating, undernourishment, heartburn, belching and a myriad of symptoms are the cause of their headache. Actually these symptoms are often incidental findings.

The gastroenterologist is often consulted because of severe headache associated with constipation which is attributed to autointoxication. These patients are high-strung sensitive individuals who think if they fail to evacuate their bowels at the accustomed time, it must be followed by headache, fatigue and

listlessness. Alvarez[20] states that it is well known that a few persons get headache when their lower bowel is filled with feces, and practically all of them get relief the minute the bowel is emptied. When they get such immediate relief, the trouble can be due to a nervous irritation of the brain and not to any intestinal autointoxication. He further states that one couldn't clean a noxious chemical out of the blood that fast and that the constipation headache bothers only those persons with a highly sensitive bowel or head, but the insensitive ones can let feces accumulate in the bowel for days or even a week or more, without experiencing any distress. The most accepted theory for this type of headache is that it is only a part of the same functional neurogenic disturbance which causes most headaches. We have all been called upon to treat the patient with functional diarrhea who complains of severe headache. Also the nervous high tension patient who has attacks of mucous colitis with severe headache whenever under emotional stress, such as going to a party, entertaining at dinner, etc. Here again, we have the instance where the headache and the gastrointestinal symptoms are both caused by a third factor other than the condition which is causing the headache. Bockus[21] noted that headache is one of the most frequent symptoms encountered by the gastroenterologist. Alimentary tract diseases, however, are not in themselves a common cause of headache except in individuals of the migrainoid-type.

Some believe that gastritis is a causative factor in migraine headache. Henning[22] found 26 per cent of 700 cases complained of this symptom. For example the so-called morning after headache with accompanying nausea and at times vomiting is due to an acute gastritis. According to Friedman[23], this may be due to tension of the neck and head muscles causing increased intracranial pressure as a result of dilatation of the cerebral vessels. Emotional stress and physical exhaustion may also be associated with this phenomenon.

Nausea and vomiting are frequently a concomitant finding with headache. The so-called "bilious headache" so termed because of vomiting bile which has been regurgitated into the stomach. Hartsock[24] believes, however, that in most cases the gastrointestinal relationship of symptoms is secondary to other factors causing the headache or to a disturbance in the central nervous system. He believes that biliary tract disease is seldom the cause of headache, and that much gallbladder surgery is done without relief but that the headache is often associated with migraine and therefore the end result is disappointing.

High intestinal obstructions which produce alkalosis will occasionally cause headache. Duodenal stasis and visceroptosis have been given as a frequent cause of headache.

Reflex headache caused by gastrointestinal dysfunction is the result of vagal irritation. This form of headache is often associated with many gastrointestinal disorders.

Toxemias associated with acute febrile conditions, such as typhoid fever and meningitis often produce headache. Equally important as an etiologic factor causing headache are the toxemias without fever noted in diseases of the liver and kidney.

Exposure to many extrinsic poisons such as carbon monoxide, arsenic or lead often cause headache and gastrointestinal symptoms.

A low blood sugar level as a cause of headache with nausea and other gastrointestinal symptoms must always be ruled out. One occasionally will find this condition associated with the migraine type of pain.

Cecal stasis caused by atony, adhesions or congenital bands are occasionally the cause of headache, although it often presents itself as a neuralgia rather than a true headache.

One of the most common forms of headache associated with indigestion is found in the constitutionally inadequate individual. In this type the patient complains of a chronically tired feeling associated with severe head pain and many vague gastrointestinal complaints, called "indigestion". This form of headache is usually caused by fatigue rather than any abdominal pathology, notwithstanding that such a headache will disappear only when the digestive symptoms have been successfully treated by rest, diet, physiotherapy, and psychiatric therapy. While pathology of the gastrointestinal system is seldom the direct cause of the headache, we can render considerable relief by treating the associated vague gastrointestinal symptoms.

Probably the most important type of headache under this heading is the so-called "tension headache". In contradistinction to the migraine headache this term should be limited to those cases which occur as a result of constant or intermittent emotional stimulation or conflict, of which the patient is more or less aware. The headache is not caused by the nervous tension per se but for the most part by the sustained muscle contractions of the head and neck muscles, together with changes in the caliber of the cranial vessels. The headache is usually bilateral and lasts for several hours or even days. At times it is constant with severe exacerbations and usually described as a dull or pressure type. It usually begins in the occipital region and is nearly always followed by mental depression. The associated symptoms are anxiety, depression, nausea and often epigastric fullness.

The patient can usually relate the specific conditions which bring on an attack, and while it can occur at the time of the severest tension state, it usually occurs afterwards, during the relaxation period. In the true tension headache there is rarely an aura, the patient is often awakened from a deep sleep with the headache, or it begins in the late evening after an especially irritating incident that had occurred during the day. Unlike the migraine patients, they do not seem to be acutely ill, and are willing to discuss their problems with you.

At times one sees a combination of the two types of headache usually called "migraine-tension headache" and the patient will volunteer the information of feeling two types of headache, the dull, often daily tension type and the severe type which occurs once or twice each month.

During the past two years my interest has been focused upon tension headaches as a result of a study of a small group of patients who have received many forms of treatment for their long-standing intractable headaches associated with depression[25]. It was thought that nicotinic acid therapy would benefit this type of headache and should be employed in those cases of tension type of headache when Ergotamine or Dihydroergotamine (Gynergen) either failed to give relief or increased the severity of the pain. Reasoning that the pain is caused by vasoconstriction of the cerebral vessels rather than dilatation of the extracerebral arteries, the vasodilator drugs would be more apt to afford relief.

We have postulated four rules which we believe necessary to follow in order to obtain satisfactory therapeutic results. 1. There is no aura. 2. The patient knows what causes the headache. 3. The headache is followed by some degree of mental depression. 4. The patient is not relieved or is made worse following the administration of Ergotamine or Dihydroergotamine (Gynergen).

While the use of nicotinic acid for the treatment of headache is not new, it has usually been given orally and in insufficient dosage which has often led to poor results and with discontinuance of the drug. Washburn[26] published encouraging results with the use of nicotinic acid in certain depressed states. The general outline of treatment which he recommended for the treatment of depressed states has been followed, but in addition, we have combined the intravenous and oral routes using a larger dosage of nicotinic acid.

Premenstrual headaches often occur in the emotional unstable individual. Where the usual drugs are of no avail, nicotinic acid therapy frequently offers excellent results and should be given about 24 hours before the onset of the headache.

Lumbar puncture is a very common cause of headache, occurring usually within a few hours, but occasionally it may occur several days later. It is characterized by pain in the occipital region, often accompanied by severe nausea and vomiting and with occasional abdominal pain.

In brain tumors the headache is often associated (occasionally even follows) severe nausea and vomiting.

Headaches associated with occular defects are often associated with gastrointestinal symptoms. Iritis, glaucoma, astigmatism, and extra occular imbalance are the chief causes.

Janeway[27] reported that hypertension is a frequent etiological factor in headache associated with gastrointestinal symptoms. In hypertensive encheph-

alopathology the headache is usually preceded by nausea and other gastrointestinal symptoms.

In syphilis the headache at times precedes the other manifestations. The headache is usually intermittent and is often accompanied by severe gastrointestinal symptoms, such as nausea, vomiting, and general abdominal discomfort. It must be differentiated from the true migraine headache.

Mention must be made of Ménière's disease, the onset of which at times begins with severe headache associated with vomiting, abdominal pain and diarrhea. Seasickness and airsickness also suggest a labyrinthine disturbance.

Patients suffering from anemia caused secondarily by disease of the gastrointestinal tract often have associated headache as a very distressing symptom. The anemia may be due to peptic ulcer, carcinoma of the gastrointestinal tract, ulcerative colitis, etc. Headache is almost invariably associated with blood dyscrasias. All of the leukemias present evidence of headache and gastrointestinal dysfunction which are often among the most distressing symptoms. Pernicious anemia with its accompanying achlorhydria may produce headaches either as a result of the anemia or fatigue. Polycythemia vera is commonly associated with severe headache especially in the early morning.

Summary

Headache is one of the most common symptoms encountered in the population. It is not only noted in the acutely and chronically ill patient, but also in people who are otherwise healthy. The association of headache with gastrointestinal symptoms have been reviewed. The importance of recognizing the various types of headache is emphasized. It is pointed out that the therapy for the different types of headache differ, and that relief may be obtained by proper treatment.

It is not intended in this paper to discuss all of the numerous causative factors of headache. The chief causes are familial, nervous, toxic, allergic, reflex, traumatic, etc. It is important to recognize that headaches often have their origin in certain organs or systems, namely cardiovascular, gastrointestinal, cerebral, blood dyscrasias, anemia, otic and occular disorders, gynecological and kidney disturbances. Besides having their origin in the above systems, they may also originate from hormonal disturbances, sugar imbalance, fatigue, worry, etc. They are often associated with many systemic diseases.

A discussion of the various forms of headache encountered by the gastroenterologist is presented in this paper. It should be emphasized that the causes of headache may be multiple and requires an understanding of the phenomena responsible for them.

REFERENCES

1. Ray, B. S. and Wolff, H. G.: Experimental Studies on Headache: Pain sensitive structures of the head and their significance in headache. Arch. Surg., **41**:813, 1940.
2. Brahms, W. A.: Abdominal Migraine, J.A.M.A., **78**:26, 1922.
3. Kleckner, M. S. and Horton, B. T.: Concurrence of Migraine and Peptic Ulcer, Gastroenterology, **13**:141, 1939.
4. Blitzstein and Brahms: Migraine with Abdominal Equivalent, J.A.M.A., **86**:675, 1926.
5. Piper, D. W.: Abdominal Migraine, M. J. Australia, **2**:468, 1951.
6. Brain, W. R.: Diseases of the Nervous System, Oxford University Press, 3rd ed., 1947.
7. Holt, L. E. and Howland, J.: Diseases of Infancy and Childhood, D. Appleton and Co., 1916.
8. Groh, R. H. and Veal, J. R.: Cranial and Abdominal Migraine, Med. Ann. Dist. Columbia, **12**:147, 1943.
9. Friedenwald, J. and Feldman, M.: Chronic Duodenal Stasis Observations in Twenty-Four Cases, Am. J. M. Sc., **178**:796, 1929. Chronische Intermittierende Duodenalstauung, Arch. f. Verdauungs. **53**:20, 1933.
10. Cunha, F. and Day, B. M.: Duodenal Stasis Caused by An Aberrant Superior Mesenteric Vessel, Am. J. Gastroenterol., **21**:121, 1954.
11. Buchanan, J. A.: The Abdominal Crisis of Migraine, J. Nervous & Mental Dis., **54**:406, 1921.
12. Moore, M. T.: Abdominal Epilepsy versus Abdominal Migraine, Ann. Int. Med., **97**:623, 1950.
13. Vaughan, W. T.: Food Allergy in the Specialties and in General Practice, Virginia Med. Monthly, **56**:725, 1930.
14. Rowe, A. H.: Abdominal Food Allergy, California & Western Med., **29**:317, 1928.
15. Thomas, J. W. and Johnston, C. R. K.: Headache of Allergic Origin, M. Clin. North America, **24**:285, 1940.
16. Friedenwald, Morrison and Morrison: Clinics on Secondary Gastrointestinal Disorder: William Wood and Co., p. 229, 1938.
17. Seigal, S.: Benign Paroxysmal Peritonitis, Ann. Int. Med., **23**:1, 1945. Gastroenterology, **12**:234, 1949.
18. Paviot, J. and Chevallier, R.: Les gastropathies allergiques. J. med. de Lyons, **17**:31, 1936.
19. Bauer, Julius: Differential Diagnosis of Internal Diseases: Grune & Stratton, p. 62, 1950.
20. Alvarez, W. C.: Functional Diseases of the Stomach and Colon, M. Clin. North America, **37**:3, 1953.
21. Bockus, H. L.: Gastroenterology, W. B. Saunders Co., Phila., p. 47, 1943.
22. Henning, Norbert: Quoted by Eusterman, G. B. and Balfour, D. G.: The Stomach and Duodenum, W. B. Saunders Co., p. 536, 1936.
23. Friedman, A. F.: Modern Headache Therapy, C. V. Mosby Co., p. 95, 1951.
24. Hartsock, C. L.: Headache of Gastrointestinal Origin, M. Clin. North America, **24**:342, 1940.
25. Morgan, Z. R.: Nicotinic Acid Therapy in Vasoconstriction Type of Headache, Maryland State M. J., **2**:7, 1953.
26. Washburn, A. G.: Nicotinic Acid and the Treatment of Certain Depressed States, Ann. Int. Med., **32**:261, 1950.
27. Janeway, T. C.: Arch. Int. Med., **12**:755, 1913.

CIRRHOSIS OF THE LIVER: ITS RELATIONSHIP TO CHOLESTEROSIS OF THE GALLBLADDER, GALLSTONES AND OTHER CONDITIONS. AN AUTOPSY STUDY*†

MAURICE FELDMAN, M.D.

and

MAURICE FELDMAN, Jr., M.D.

Baltimore, Md.

In recent years there has been considerable impetus regarding the function of the liver in the synthesis of cholesterol. In as much as a disturbance of cholesterol metabolism plays a major role in cardiovascular diseases and in cholesterosis of the gallbladder, it was thought that the fat imbalance produced by the liver might play a significant role in the etiology of cholesterosis of the gallbladder and gallstones. Although there have been many studies on the relationship of gallstones in liver disease, a perusal of the available literature revealed little or no investigative research on its relationship with cholesterosis of the gallbladder.

The incidence of Laennec's cirrhosis of the liver varies from 2.4 to 18.6 per cent, depending upon the source of material. In 1,319 consecutive adult autopsies, we found 49 cases of Laennec's cirrhosis, an incidence of 3.7 per cent. In 29,779 autopsies, Lieber found 726 cases of portal cirrhosis, an incidence of 2.4 per cent. On the other hand, Spigolon, in 5,921 necropsies noted an incidence of 18.6 per cent.

It is well known that the liver plays a significant role in lipid metabolism. There is much evidence to show that the liver synthesizes and excretes cholesterol. The liver is believed to be a sorting point for the fatty acids and a central laboratory in which phospholipids are assembled[2]. Cholesterol is esterified, synthesized, stored, as well as destroyed by the liver[13]. One of the major causes of changes in the blood levels of cholesterol and cholesterol esters is hepatic and biliary disease[9]. An increase in total cholesterol in the liver, chiefly the esterified fraction, is known to occur in fatty livers produced experimentally in animals by dietary means. Ramalingaswami et al observed that there is no direct correlation between the amount of cholesterol and the severity of fatty infiltration of the liver. They believe that there is a specific disturbance of cholesterol metabolism in this condition. It has also been reported that the

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†From the Sinai Hospital, Baltimore, Md.

We are indebted to Dr. Tobias Weinberg, Head of the Department of Laboratories of the Sinai Hospital, for the privilege of using the autopsy material.

pancreatic factor, lipocaic, has a specific preventive effect on the deposition of cholesterol in the liver of animals.

According to Henegar and Turner, parenchymatous liver disease is usually associated with a decreased value for total cholesterol and esters fraction. They noted that the amount of esterified cholesterol is roughly proportionate to the degree of liver damage and as such has considerable prognostic value. In Laennec's cirrhosis, the serum cholesterol value varies with the stage of the disease at the time of the investigation. In uncompensated cases, the total serum cholesterol and cholesterol esters remain normal. In Hall et al, studies of portal cirrhosis, tested 111 times for cholesterol values, they noted that cholesterol was decreased in 34, increased in 10, and was normal in 67 cases. In 71 tests for cholesterol esters, the determinations yielded a decrease in 41 cases and normal values in 31 instances. In cases of alcoholic cirrhosis, complicated by hepatitis and fatty livers, Lichtman noted the total cholesterol varied

TABLE I

THE INCIDENCE OF GALLSTONES IN LAENNEC'S CIRRHOSIS OF THE LIVER

	Cases	Gallstones	Per Cent
Lieber	726	133	18.0
Rolleston and McNee			13.0
Rabl			12.5
Bucalo	500		13.0
Feldman	49	16	32.6

from 260 to 400 mg. per cent; cholesterol esters from 40 to 50 mg. per cent; free cholesterol from 130 to 240 mg. per cent, and total phospholipids from 110 to 370 mg. per cent.

For the purpose of our research studies of the relationship of cholesterosis of the gallbladder with liver disease, it was thought that the investigation of anatomic specimens of autopsy material might be the best means to evaluate the etiologic factors involved, as well as to determine the incidence of this relationship. Bagnoli and Monaci, in their studies on cirrhosis of the liver, noted a passive hyperemia, dilatation, hyperplastic regressive lesions and thrombosis, due to local venous stasis of the veins in the wall of the gallbladder. Besides the above changes, they also noted a stagnation of the absorption of intramural lipids. Their pathologic findings strongly suggest the possibility that such changes as they record might form an etiologic basis for the production of cholesterosis of the gallbladder.

In a study of 1,319 consecutive adult autopsies, we found 165 cases of cholesterosis of the gallbladder, an incidence of 12.5 per cent. On the other hand, among the 1,319 autopsies there were 49 cases of Laennec's cirrhosis of the liver, and among these there were only 2 instances of cholesterosis of the gallbladder, an incidence of 4 per cent. In the same autopsy studies we also found 12 cases of biliary cirrhosis of the liver, and among these, we did not find a single instance of cholesterosis of the gallbladder. From these autopsy data, it can be definitely stated that cholesterosis of the gallbladder is not caused by liver disease (Laennec's cirrhosis) and that the two conditions are unrelated.

TABLE II

THE INCIDENCE OF VARIOUS COEXISTING CONDITIONS FOUND TO BE ASSOCIATED WITH LAENNEC'S CIRRHOSIS AND BILIARY CIRRHOSIS OF THE LIVER

	49 Cases Laennec's Cirrhosis	12 Cases Biliary Cirrhosis
Gallstones	16	6
Cholesterosis of gallbladder	2	0
Cholecystitis	3	1
Cancer of liver	3	1
Adenoma of liver (bile duct)	2	1
Splenomegaly	16	1
Varices of esophagus	17	2
Pancreatic cyst	2	1
Pancreatic stones	1	0
Pancreatitis	1	0
Diabetes	3	2
Duodenal ulcer	2	1

In our 49 cases of Laennec's cirrhosis of the liver we found only 3 instances of cholecystitis. Ratnoff and Patek in a study of 386 cases of cirrhosis of the liver, found 3 per cent with evidence of cholecystitis. They do not mention, however, whether there were any cases of cholesterosis of the gallbladder among them.

The incidence of the association of gallstones in liver disease has been established by many authorities. It would seem reasonable to believe that the formation of gallstones may originate as a consequence of some liver disease, but this theory of the formation of gallstones has not been fully established. Since we have found a low incidence of cholecystitis and cholesterosis of the gallbladder associated with our autopsied cases of Laennec's cirrhosis of the

liver, it was thought that the incidence of gallstones would be lower in these cases, since some degree of chronic cholecystitis is commonly associated with gallstones. This assumption, however, proved to be erroneous, as our autopsy studies revealed a higher incidence among these cases. According to Rabl, Lichtman, and others, the incidence of gallstones is higher in patients with cirrhosis of the liver than in the controls. In a study of our 1,319 adult autopsies, gallstones occurred in 22.7 per cent of cases, while in the 49 cases of Laennec's cirrhosis, 16 revealed gallstones, an incidence of 32.6 per cent. Although the difference in the incidences in our cases of cirrhosis is 10 per cent higher than we found in the general autopsy adult population, the number of cases is too small to evaluate, and for this reason may not be statistically significant. Bucola compared the incidence of gallstones in 500 cases of Laennec's cirrhosis and 500 controls, noted an incidence of 13 per cent in both groups, concluded that

TABLE III

THE INCIDENCE OF HEPATOMEGALY AND SPLENOMEGALY IN LAENNEC'S CIRRHOSIS OF THE LIVER

		Hepatomegaly		Splenomegaly	
	Cases	Cases	Per Cent	Cases	Per Cent
Douglas and Snell	444	315	70.9	143	32.2
Del Greco et al	121	71	58.7	62	51.2
Hall et al					65.0
Feldman	49			16	32.6

Laennec's cirrhosis of the liver and cholelithiasis are unrelated conditions (Table I).

Besides the cases of gallstones and cholesterosis of the gallbladder associated with cirrhosis of the liver, various other conditions were noted in our autopsied cases. These are shown in Table II.

Hepatomegaly and splenomegaly are commonly observed to be associated with cirrhosis of the liver. According to Kelsey et al cirrhosis of the liver, when associated with portal congestion, produces a high incidence of splenomegaly. Table III shows the incidence of these conditions.

Esophageal varices is commonly associated with liver disease. In our 49 cases of Laennec's cirrhosis, it occurred in 17 instances, an incidence of 34.7 per cent. The incidence of esophageal varices in fatal cases is almost twice as high as in the non-fatal cases. In Bjorneboe and Raaschou's 76 cases of cirrhosis, esophageal varices occurred in 24 or 58 per cent; and in Brick and Palmer's 150 cases, 95 or 63.3 per cent revealed evidence of varices.

Summary

Since it has been established that cholesterol and cholesterol esters are synthesized and excreted by the liver, it has been assumed that there might be some relationship between liver disease, cholesterosis of the gallbladder and gallstones. Our autopsy study has shown that the liver apparently plays no significant role in the production of cholesterosis of the gallbladder. Cholesterosis of the gallbladder occurred in only 4 per cent of cases with Laennec's cirrhosis of the liver, whereas, cholesterosis of the gallbladder occurred in 12.5 per cent in our adult autopsy population. Although the incidence of gallstones among cirrhotic liver cases is slightly higher than in the non-cirrhotics, this may not be statistically significant. Since there is little increase in the incidence of gallstones in cirrhotic patients, one must assume that gallstones are not produced by liver disease. It has also been assumed by many that cholecystitis is a precursor of gallstones. In our studies of Laennec's cirrhosis of the liver, the incidence of demonstrable cholecystitis and cholesterosis of the gallbladder was extremely low, but in spite of this, the incidence of gallstones was rather high. One might speculate on the possibility that there may have been a slight inflammatory process of the gallbladder at the time when the gallstones originated, but the signs of inflammation might have disappeared by the time of death when these studies were made. From the data presented, it appears that there must be some intrinsic gallbladder disturbance to account for the etiology of cholesterosis and gallstones.

It is interesting to point out that in liver disease, the cholesterol values may be either decreased or normal. Cholesterol determination among our cases of cholesterosis of the gallbladder have likewise shown no significant change to indicate that the liver is involved in this condition.

BIBLIOGRAPHY

Bagnoli, S. and Monaci, M.: Venous and Dystrophic Changes in the Absorption of Lipids in the Wall of the Gallbladder, Accompanying Cirrhosis of the Liver. Arch. "De Vecchi" Anat. patol., **18**:455, 1952.

Balfour, W. M.: Human Plasma Phospholipid Formation, A Study Made with the Aid of Radiophosphorus. Gastroenterology, **9**:686, 1947.

Bjorneboe, M. and Raaschou, F.: Pathology of Subchronic Atrophy of Liver: Comparison with Cirrhosis Hepatitis Laennec. Arch. Int. Med., **84**:933, 1949. Acta med. Scand., Supp. **234**:41, 1949.

Brick, I. B. and Palmer, E. D.: Incidence and Diagnosis of Esophageal Varices in Cirrhosis of the Liver: An Esophagoscopic Study. Gastroenterology, **25**:378, 1953.

Bucalo, H. D., Jr.: The Incidence of Cholelithiasis in Laennec's Cirrhosis of the Liver. Am. J. M. Sc., **224**:619, 1952.

Del Greco, F., Maffei, R. and Malizia, E.: Laennec's Cirrhosis of the Liver: Clinical and Statistical Study of 121 Cases. Settim med., **40**:78, 1952.

Douglas, B. E. and Snell, A. M.: Portal Cirrhosis: An Analysis of 444 Cases with Notes on Modern Method of Treatment. Gastroenterology, **15**:407, 1950.

Feldman, M. and Feldman, M., Jr.: Cholesterosis of the Gallbladder. An Autopsy Study of 165 Cases. Gastroenterology, **27**:(Nov.), 1954.

Hall, E. M., Olsen, A. Y. and Davis, F. E.: Portal Cirrhosis; Clinical and Pathologic Review of 782 Cases from 16,600 Necropsies. Am. J. Path., **29**:993, 1953.

Henegar, G. C. and Turner, J. L.: Medical Progress in Cholesterol Metabolism in Relation to Diseases of the Liver and Biliary Tract. Calif. Med., **73**:489, 1950.

Kelsey, M. P., Robertson, H. E. and Giffin, H. Z.: The Role of Chronic Thrombosis of the Portal Vein and Its Tributaries in the Syndrome of Splenic Anemia. Surg. Gynec. & Obst., **85**:289, 1947.

Lichtman, S. S.: Diseases of the Liver. 2nd ed. Lea & Febiger, Phila., 1949. pp. 254, 579.

Lieber, M. M.: The Incidence of Gallstones and Their Correlation with Other Diseases. Ann. Surg., **135**:394, 1952.

Peters, J. P. and Van Slyke, D. D.: Quantitative Clinical Chemistry Interpretations. Williams & Wilkins Co. Balto. 1946. 2nd ed. Vol. 1. p. 456.

Rabl, R.: Geographisch-pathologische Untersuchungen über Ikterus akute gelbe Leberatrophie, Leberzirrhosen und Cholelithiasis Ein Beitrag zu ihren Ursachen und Krankheitsbeziehungen. Arch. f. Schiffs. u. Tropen-Hyg., **38**:3, 1934.

Ramalingaswami, V., Sriramachari, S. and Tulpule, P. G.: Hepatic Cholesterol Content in Nutritional Disorders. Lancet, **2**:661, 1952.

Ratnoff, O. D. and Patek, A. J. Jr.: The Natural History of Laennec's Cirrhosis of the Liver. Medicine, **21**:207, 1942.

Rolleston, H. D. and McNee, J. W.: Diseases of the Liver, Gallbladder and Bile Ducts. MacMillan, London, 3rd ed. 1929. p. 238.

Spigolon, G.: A Statistical Study of Certain Hepatic and Biliary Conditions. Arch. ital. mal. app. digest., **18**:151, 1952.

Discussion

Dr. A. Allen Goldbloom (New York, N. Y.):—I want to ask Dr. Feldman whether other determinations besides cholesterol were made in his cases of cirrhosis with jaundice. Cirrhotic livers without jaundice may present a practically normal serum lipid value.

Cholesterosis of the gallbladder may be a metabolic disturbance, since we know that cholesterosis may exist for years without producing any gallstones. (Held, I. W., and Goldbloom, A. A.; Functions of the Gallbladder, M. Clin. North America; **13**:515, 1929).

I suggest to the members of this organization that they go on with the trend. I am sure most of us today do not consider cholesterol itself as evidence of lipid disturbance. One may have a normal cholesterol value while the other lipid partitions may be disturbed. All serum lipid fractions must be determined to evaluate a true disturbance in lipid metabolism. (Goldbloom, A. A.: Clinical Studies of Blood Lipid Metabolism. 1. Normal Blood Lipid Variations of Phospholipids, Neutral Fats, Total Lipids, and Lipid Fraction Percentages; Am. J. Digest. Dis., **19**:9, 1952).

Our work at the New York Medical College, Flower-Fifth Avenue Hospitals —has definitely shown there is a distinction between the cholesterol and the other lipid partition disturbances, whether jaundice is present or not. (Goldbloom, A. A., Eiber, H. B. and Boyd, L. J.: Clinical Studies in Blood Lipid Metabolism. VIII. Disturbed Serum Lipid Partitions in Liver Disease with and without Jaundice. Am. J. Digest. Dis. **20**:354, 1953).

As gastroenterologists and clinicians, we must make a distinction whether jaundice is present in our cases of cirrhotic patients, since jaundice per se may produce a disturbance in cholesterol (Goldbloom, A. A., Eiber, H. B. and Boyd, L. J.: Clinical Studies of Blood Lipid Metabolism X. Serum Lipid Partitions in Metabolic Diseases. Am. J. Gastroenterol. **22**:27, 1954).

Dr. Feldman:—Our studies on cirrhosis of the liver were made from pathologic material and are statistical considerations of this subject from a pathological point of view. No clinical studies were made of these cases, and therefore I cannot answer Dr. Goldbloom's question as to whether there was jaundice in any of our cases. We have pointed out that there is no relationship between cholesterol determinations of the blood and bile cholesterol, and emphasized that cholesterosis of the gallbladder is apparently a localized condition involving only the gallbladder without systemic involvement.

RETENTION CYST OF LIVER CAUSED BY OPISTHORCHIASIS ASSOCIATED WITH CARCINOMA

Case Report

VIKIT VIRANUVATTI, M.D., M.P.H.T.M.
DHANYASOBHAK KSHEMSANT, M.D.
and
NATTH BHAMARAPRAVATI, M.D.
Bangkok, Thailand

Cyst of liver is a rare morbid condition and is generally classified into parasitic and nonparasitic cysts[1]. Parasitic cyst of liver caused by opisthorchiasis has never been mentioned in any text books and medical literatures. Recently V. Viranuvatti and S. Mettiyawongse[2] reported a case of retention cyst of liver caused by *opisthorchis viverini* associated with carcinoma admitted to Siriraj Hospital, Bangkok in 1951. We have come across a similar case recently and think it is worthwhile to publish this additional record.

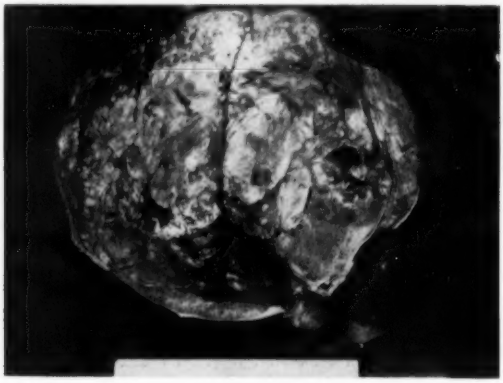

Fig. 1—Cut surface of the liver showing the dilated cystic bile duct on the right.

Case Report

A 33-year old married Thai farmer residing in the northeastern part of Thailand was admitted to the Medical Service on 18 November 1953 with the chief complaint of a mass in the right hypochondrium for two months.

Present illness:—The patient had been well until three months prior to admission when he developed oppression and dull feeling in the right hypo-

From the Department of Medicine and Pathology, Siriraj University Hospital, Bangkok Thailand.

chondrium while digging. This became persistent. One month later, he noticed a mass under the right costal margin with pain radiating to the right shoulder and scapula. He then became progressively weak with nausea and loss of appetite. The patient later passed three to four bowel movements daily with reddish-brown, foul-smelling stools. His relatives noticed yellowish discoloration of the skin and conjunctiva. Fifteen days later the mass became harder and tender with onset of feverish sensation. Urine became darker in color with some urgency. Anorexia and weakness became more marked. The patient was then brought for hospitalization.

Past history revealed dysentery ten years ago, and fever with chills eight years ago.

Personal history revealed poorly nourished condition, consuming ravine water, uncooked fishes and occasional local drinks.

Physical examination on admission revealed a thin, debilitated, anemic and mildly jaundiced man with hepatic facies. Temperature 37.7°C., Pulse 104/min., Blood Pressure 120/90 mm. Hg., Respiration 20/min., Lips showed excoriation, tongue was coated, tonsils were enlarged. The abdomen showed moderate guarding. Liver was enlarged about 10 cm. under the costal margin in M.C.L. with anterolateral bulge especially below the costal margin. Liver was enlarged upwards to the level of fourth intercostal space anteriorly in M.C.L. The surface was smooth. Tenderness was elicited over the bulging area. Lower right intercostal spaces were widened with slight diminished breath sounds. Others were not contributory.

Laboratory findings:—

	1953	18 Nov.	20 Nov.	23 Nov.	28 Nov.
Blood:	Hgb.	60%	60%	60%	65%
	R.B.C.	4.8 ml.	3.4 ml.	3.2 ml.	4.2 ml.
	W.B.C.	8400	8600	9400	7600
	Polys.	88%	82%	80%	72%
	Lymp.	12%	18%	20%	26%
	Eos.	—	—	—	2%
	Malaria	neg.	neg.	neg.	neg.
Urine:	Character	turbid	turbid	clear	clear
	Sp. Gr.	1.020	1.020	1.006	1.012
	Albumin	1+	1+	neg.	neg.
	Bile	neg.	neg.	neg.	neg.

Stools: R.B.C. 15/H.D., W.B.C. 20/H.D.; positive for Trichomonas hominis and Opisthorchis ova; Stoll's egg count for Opisthorchis ova 4,127,000 eggs/day.

Blood Chemistry:—19 Nov.: Albumin 3.5 gm./100 c.c., globulin 2.1 gm./100 c.c., sugar 69 mg./100 c.c., urea 38.3 mg./100 c.c., creatinine 1.4 mg./100

cc., icterus index 21.2, direct acting bilirubin 1.4 mg./100 c.c., indirect acting bilirubin 2.1 mg./100 c.c., D/I ratio 66.7.

25 Nov.: Total blood cholesterol 180 mg./100 c.c., alkaline phosphatase 5.88 B.U., serum amylase 102.84.

4 Dec.: Icterus index 111.0 (one day before death).

Liver Function Tests:—C.C.F. 2+, T.F. 1+.

Blood Kahn:—negative.

In the out-patient clinic, the provisional diagnosis of "amebic liver abscess" was made and the diagnostic aspiration was performed yielding on the first suction a clear colorless fluid and later rice-water colored fluid totaling about 20 c.c. Microscopic examination revealed five adult opisthorchis and numerous ova. Twenty c.c. of 70 per cent Pyelosil was instilled in the cavity for the x-ray visualization. After admission symptomatic and supportive measures were given.

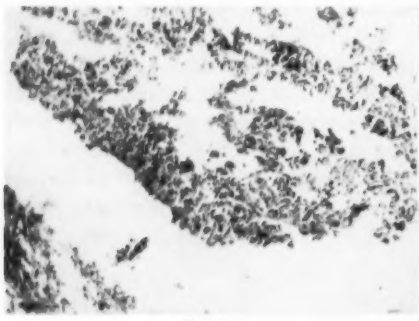

Fig. 2

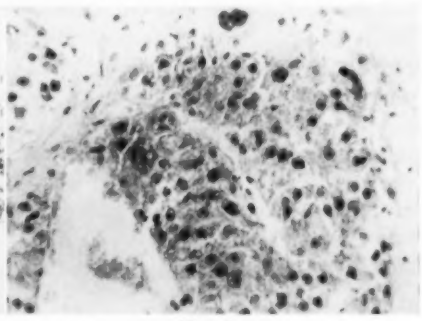

Fig. 3

Fig. 2—Carcinoma of liver (x 100).
Fig. 3—High power magnification showing islands of polygonal-shaped cells with hyperchromatic nuclei and numerous mitosis.

Two additional aspirations were performed transabdominally yielding 30 and 150 c.c. of fluid consecutively. Specimens of the aspirated fluid were studied.

Aspirated Fluid: 1953	18 Nov.	24 Nov.	26 Nov.
Character	clear, whitish and slightly turbid.	slightly yellow, turbid.	blood and bile colored.
Amount	20 c.c.	30 c.c.	150 c.c.
Adult Opisthorchis	5	—	—
Micros. R.B.C.	—	—	150/H.D.
W.B.C.	2-3/H.D.	2-3/H.D.	10/H.D.
Opisthorchis ova	numerous	neg.	neg.

Biochemistry of fluid:—18 Nov. Protein 1.1 gm./100 c.c., Albumin 0.7 gm /100 c.c., Chloride 585 mg./100 c.c., Bile—neg., Sugar—trace.

X-ray film of the liver region showed opaque medium filled in the cystic cavity size about 7 x 4 cm. The liver is enlarged. Right dome of diaphragm is elevated and fixed under fluoroscopy.

Impression:—Cyst of liver size about 7 x 4 cm. (18 Nov.).

Repeated P.A. film of the liver region showed complete disappearance of the opaque medium previously visible over the liver region (24 Nov.).

Liver biopsy was performed and sent for histological study; but the tissue was inadequate for diagnosis.

Despite supportive and symptomatic treatment, the patient gradually became deeply jaundiced, ran a low grade fever and later, lapsed into hepatic coma and died on 5 Dec. 1953.

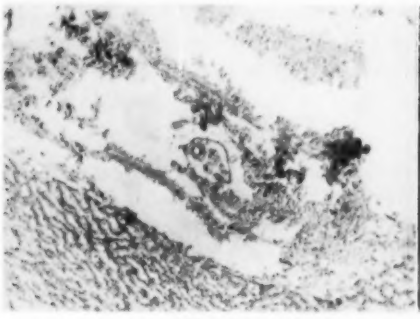

Fig. 4

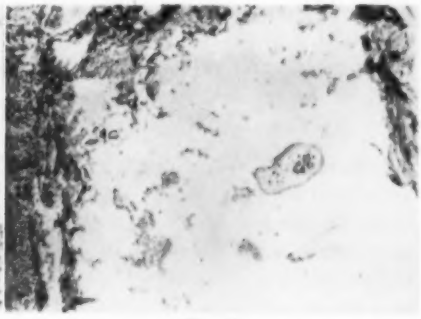

Fig. 5

Fig. 4—Cut section through the worm showing uterus containing numerous eggs and cellular reaction with liver cell cords (x 100).

Fig. 5—Cut section showing part of the worm and some areas of necrosis (x 50).

Autopsy findings:—Autopsy shows a man of sturdy build, without evidence of any disease externally. The liver is much enlarged, about 3,000 gm. in weight. It is firm, and bile-stained, slightly nodular in appearance. Cut sections reveal dilated intrahepatic ducts which contain large number of *Opisthorchis viverini*. A major portion of right lobe is replaced by grayish-white growth, in which numerous foci of necrosis are seen. The gallbladder is distended, and filled with dark red bile. There is nearly complete obstruction of cystic duct due to external pressure from a portion of growth. A total number of more than 4,000 of adult *Opisthorchis viverini* are recovered from the liver.

Other organs show nothing remarkable.

On microscopic examination, the growth is found to be composed of cords and islands of polygonal shaped cells, with oversized hyperchromatic nuclei and granular pinkish cytoplasm. The arrangement more or less resembles liver cell cords. Numerous mitoses are seen. The surrounding liver tissue in the imme-

diate vicinity of the growth is atrophic and necrotic focally, whereas that in the remote area shows increased fibrosis especially in the portal areas. The biliary canals are hyperplastic and dilated, containing sections of parasites and their ova and also some bile thrombi. Numerous lymphocytes and plasma cells are seen infiltrating around these bile canals.

Comment:—The provisional diagnosis of "amebic liver abscess" in this case was made on the basis of enlarged bulging cystic liver. The first aspiration yielding clear colorless fluid with enormous amount of ova and five adult *Opisthorchis viverini* points to the diagnosis of retention cyst caused by the parasites. Autopsy revealed dilated bile ducts as shown in figures, from which a very large number of adult *Opisthorchis viverini* were recovered. The adult worms may block the lumen of bile ducts and capillaries causing retention cyst or pseudocyst formation, which may collapse after aspiration and later become not clearly visible at autopsy. By the motility, irritation and tissue reaction from the enormous number of the parasites may block the lumen of bile ducts causing retention cyst formation. Another finding whether coincidental or bearing some relationship, is the primary liver cell carcinoma found in the other site of liver well separated from the site of parasites.

Summary:—An additional case of retention cyst caused by opisthorchiasis associated with carcinoma with autopsy report is presented in detail. The differential diagnosis from liver abscess and nonparasitic cyst of liver is stressed. The diagnosis is made by the finding of liver fluke ova in the aspirated fluid. Opisthorchiasis as a cause of retention cyst of liver should be suspected in endemic area where infestation is prevalent.

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REFERENCES

1. Jones, J. F. X.: Removal of Retention Cyst from Liver. Ann. Surg. **77**:68, 1923.
2. Viranuvatti, V. and Mettiyawongse, S.: Observation on two cases of Opisthorchiasis in Thailand. Ann. Trop. Med. Parasit., **47**:291, 1953.

THE SURGICAL TREATMENT OF CHRONIC RELAPSING PANCREATITIS*

I. RIDGEWAY TRIMBLE, M.D.

and

HUGH P. CURTIS, M.D.

Baltimore, Md.

Two cases are reported of chronic pancreatitis, associated with diffuse lodgment of stones throughout the pancreas, characterized symptomatically by continuous, disabling pain. The causative factors for this condition are discussed; the alternative surgical possibilities for correction are considered and the actual operative procedures which were selected are described.

Pancreatitis, either in its acute or chronic form, is a common disease and varies in intensity from mild attacks to a fulminating catastrophe. Fortunately,

Fig. 1—Case 1. Entire pancreas studded with multiple small areas of calcification. (Small rubber tube over right twelfth rib level.)

the latter type occurs in only a small proportion of the total cases. Recurrence is common and may be anticipated. With repeated attacks there may be progressive damage or destruction of the gland with resulting deficiencies in external and internal secretion. Diffuse deposit of calcium salts or stones is observed in over half of the cases, indicating the severity and long duration of the disease. On the other hand, strangely enough, in some patients after many years of recurrent attacks no demonstrable changes may be found in the pancreas.

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Frequently, but not always, pancreatitis is associated with biliary tract disease. Many disorders, heretofore called postcholecystectomy syndrome, biliary dyskinesia, etc., are actually recurrent attacks of pancreatitis.

A disturbing feature in this whole problem is that the etiology, and therefore the treatment, remain controversial.

The frequent association of pancreatitis with disease of the biliary tract, especially cholelithiasis, was noted by Körte[1] in 1899, and he thought that in-

Fig. 2—Case 2. Pancreas is outlined by multiple calcium deposits.

flammation extended down the common bile duct to enter the pancreas. The possibility that gallstones lodged in the ampulla of Vater could cause disease of the pancreas by obstructing the main pancreatic duct was first suggested that same year by Lancereaux[2], who speculated that a stone so lodged might produce conditions favorable to the penetration of mirco-organisms into the pancreas.

Opie[3], in 1901, however, is given the credit for the theory that the cause of pancreatitis in a large proportion of the cases is due to the reflux of bile up the main pancreatic duct, caused by the lodgment of a stone in the ampulla

of Vater, converting the common bile duct and pancreatic duct into a continuous channel. Normally, of course, the common bile duct and the pancreatic duct, run as separate channels and then unite and open by a common orifice upon the summit of the duodenal papilla. The short tube formed by the union of the two ducts is dilated into an ampulla, the ampulla of Vater.

Opie also noted that acute pancreatitis had been caused in dogs by the injection of dilute hydrochloric acid or of gastric juice into the pancreatic duct. He injected bile into the pancreatic duct and obtained a necrotizing, hemorrhagic inflammation of the pancreas. Those who support the common channel, reflux of bile theory as the cause of pancreatitis believe that the bile thus admitted causes an activation of trypsinogen and lipase.

TABLE I

ETIOLOGY OF PANCREATITIS

1. Infection of pancreas by lymphatic or blood stream spread.
2. Obstruction of ampulla of Vater by a calculus.
3. Obstruction of pancreatic duct itself.
4. Spasm at the sphincter of Oddi.
5. Protein deficiency.
6. Repeated vascular disturbances of pancreas.
7. Miscellaneous.
   a. Direct blow.
   b. Operative removal of duodenal ulcer.
   c. Exploration of common duct at ampulla.

This general idea that the cause of pancreatitis is in some way closely connected with gallstones persists today and is, no doubt, responsible for a large percentage of cases with this disease. Many of our patients with pancreatitis, however, do not have gallstones and have not suffered with demonstrable bile tract infection.

In this connection Nordman[4] closed the papilla of Vater by purse string suture. Only jaundice developed with dilatation of biliary and pancreatic ducts. Bile entered the common duct without apparent harm. If then infected material was injected into the gallbladder, typical necrosing pancreatitis developed. Luim and Maddock[5] have induced pancreatitis in experimental animals by ligating the pancreatic duct and then stimulating this gland through the vagi or the blood stream.

Certainly, with slowly developing stenosis of the common duct or of the ampulla of Vater, as in carcinoma of the head of the pancreas or of the ampulla, one does not encounter acute pancreatitis. The body and tail of the pancreas, behind the carcinoma at the head, however, are often the seat of a hard, diffuse pancreatitis.

In 1913, Archibald[6] pursued from a somewhat different angle this same theory of regurgitation of bile as a cause of pancreatitis. He called attention to the description by the Italian physiologist, Oddi, in 1887 and 1888 of a sphincter muscle at the papilla of Vater, which Oddi found in dogs could resist a pressure of 50 mm. of mercury and which could be put into spasm by mechanical irritation of the duodenal mucosa or by the application of dilute hydrochloric acid in either the duodenum or stomach. He also found that stimulation of the vagus nerve produced a very prompt and intense contraction of this sphincter. Although this work was done in 1887, there was nothing in the surgical literature for the next 30 years until Archibald commenced writing about it in 1913.

He insisted that the keynote of the treatment of pancreatitis lay in the relief of pressure in the biliary system, the release of a safety valve, thus giving the pancreatitis a chance to subside naturally. He advised that a cholecystostomy

TABLE II

SURGICAL PROCEDURES

1. Mandatory
   a. Removal of stones from biliary tract if present.
   b. Relief of jaundice if present.
2. Selective
   a. Operations on sympathetic nerves.
   b. Gastric resection.
   c. Pancreaticolithotomy.
   d. Resection of the pancreas.
   e. Anastomosis of the duct of Wirsung.
   f. Sphincterotomy.
   g. Transplantation of the common duct.

be done in patients with pancreatitis, and that this cholecystostomy be maintained for at least 3 months.

Pursuing this idea of the regurgitation of bile into the pancreatic duct caused by spasm of the sphincter of Oddi, Archibald[7] as far back as 1919 first cut this sphincter in a patient with recurrent pancreatitis. In recent years this same procedure has been reemphasized and strongly recommended by Doubillet and Mulholland[8].

Clinically, obstruction at the ampulla of Vater, a channel common to both pancreatic juice and bile, may be caused not only by a calculus or by spasm of the sphincter but also by a plug of mucus or inflammatory debris, edema, a tumor, a parasitic worm. Acute pancreatitis can occur, however, in the absence of an anatomically demonstrable common channel for pancreatic juice and bile, and this absence has been estimated to occur in 20 to 30 per cent of normal subjects. In these subjects, obstruction of the pancreatic ductal system alone may be produced by a tumor, a calculus, squamous metaplasia as described by

Rich and Duff[9], the inflammation and edema caused by a penetrating duodenal ulcer, inversion of the duodenal stump during gastric resection, or by spasm of the duodenum or of the sphincter surrounding the opening of the pancreatic duct. In such instances, the absence of a common channel for bile and pancreatic juice apparently eliminates the possibility that bile activates the enzymes believed to be responsible for some of the pathological changes. An excellent study of the normal variations in the extrahepatic and pancreatic ducts was made by Rienhoff and Pickrell[10] in 1945. Recent observations by Hicken and McAllister[11], however, suggest that reflux of bile into the pancreatic duct can occur regardless of the type of anatomic arrangement of the terminal portions of the common bile and pancreatic ducts.

The occurrence of attacks of acute pancreatitis 2 to 3 hours after the ingestion of a heavy meal or an over-indulgence in alcohol has led to the belief that these are important precipitating factors because of their ability to incite an increased secretion of enzymes. Alcohol is believed to cause pancreatitis by stimulating the pancreas to secrete a larger volume of pancreatic juice against an obstruction to the flow of secretion caused by spasm and edema of the papilla of Vater.

In an excellent recent abstract on pancreatitis, Machella[12] states that the question has been raised as to whether or not human malnutrition, and specifically protein deficiency, may play a role in pancreatic disorders, especially from the standpoint of interfering with enzyme formation. This possibility is based on the production of acute pancreatitis in rats, dogs, cats, and monkeys by ethionine, the ethyl analog of methionine, and the inhibition of this action by methionine. Ethionine has been found to inhibit the incorporation of radioactive methionine into the proteins of some tissues and therefore may perhaps inhibit some aspects of protein synthesis.

The production of acute pancreatitis in dogs by the prolonged daily administration of mecholyl suggests the possibility that repeated and profound vascular disturbances as a result of autonomic imbalance may be factors in the production of acute or recurrent pancreatitis. In fact, in some patients, attacks of acute pancreatitis do appear to occur during emotional storms and upheavals.

Acute pancreatitis has also been known to follow a direct blow on the abdomen, trauma incident to manipulation of a peptic ulcer during laparotomy, transduodenal exploration of the common duct, occlusion of the pancreatic arterial system by arteriosclerosis or polyarteritis nodosa, and has occurred as a complication of mumps and scarlet fever[13].

A common etiology for all cases of pancreatitis has not generally been accepted. It has, however, been fairly well established experimentally that the inflammatory process can be initiated by preventing the external secretion of

an actively stimulated gland from entering the duodenum[5]. The resultant increased pressure in the ductal system leads to distention and rupture of the acini and smaller ducts, and permits pancreatic juice to escape into the pancreas itself and the tissues around it. The necrosis of the pancreas and of the surrounding fat has been attributed to their digestion by trypsin, the enzyme which is released by activation of the trypsinogen in the pancreatic juice. The mechanism by which trypsinogen is activated is not satisfactorily established.

Medical Management

A reasonable attempt with careful medical management is the proper course before surgical intervention is advised. Exceptions to this rule are made when cholelithiasis has been demonstrated and when there is a fair suspicion of carcinoma of the pancreas. Then exploration is indicated in order to eliminate the associated disease in the biliary tract and to examine the pancreas directly.

Medical measures include a bland diet, low in fats, free of raw fruits and vegetables. Alcohol should be prohibited. Antispasmodics and mild sedatives are employed; Banthine may help. Every effort must be made to eliminate the use of narcotics. Morphine is especially bad since it induces spasm at the sphincter of Oddi; many of these patients become drug addicts. Pancreatin has proved most helpful in alleviating the deficiency of the external secretion of the pancreas. A minimal dose of 6 to 8 gm. a day is advisable. The state of glucose metabolism should be determined and treated by diet and insulin if necessary.

Some patients who do reasonably well between attacks may be helped during the acute episodes by gastric suction, doses of atropine, and by splanchnic novocaine blocks.

The first patient, C. R. J., was a white male of 31 years who had been having attacks of severe abdominal pain for 8 years, starting in 1945 while serving in the U. S. Navy. They were located in the right upper abdominal quadrant, about 6 cm. from the midline, beneath the costal margin, and radiated directly through to the back. For the first five minutes after onset they were most severe, they were relieved somewhat by lying down. For the past 18 months, since January, 1952, they were much more intense, and incapacitated him for work 50 per cent of his time. Placement on a low fat diet and giving of pancreatin in June 1952 had given definite relief. He rarely drank any alcoholic beverage.

Nausea and vomiting would occur with the attacks. His stools became foamy, bulky, and foul smelling but retained a bile color. He had never been jaundiced. An exploratory laparotomy had been done in 1946. He was referred to us with the suggestion that a splanchnicectomy be done to relieve his pain.

His examination at Mercy Hospital, Baltimore, on 2 February 1953, showed an alert, intelligent, active, very thin male of 31 years. The abdomen showed a

healed upper right rectus scar, no abnormal masses, some tenderness in the upper right quadrant. No jaundice. Blood showed hemoglobin 15 gm., 4,600 white blood cells, sugar 105 mg. per cent, cholesterol 224 mg. per cent, total bilirubin 0.5 gm. per cent, cephalin flocculate negative. X-ray of the abdomen showed multiple calcified areas throughout the pancreas and a normal gallbladder. No abnormality was present on x-ray of the stomach or duodenum. Preoperative impression was chronic pancreatitis with pancreaticolithiasis.

The second patient, A. C., was a Negro male, aged 41 years, admitted to The Baltimore City Hospitals, 6 January 1954, complaining of upper abdominal pain of two years' duration. At first the pain was intermittent; it would come on in cramps. During the 6 months previous to admission it became steady and involved the epigastrium and left subcostal region, radiating to the left costovertebral angle. In recent weeks the pain went straight through to his back. Usually it appeared one-half to one hour after eating, and would last for variable periods. Two years before, the attacks were about one month apart, but in the last 6 months, before admission they became more frequent and seemed to occur about twice a week. In more recent months a dull pain had persisted almost constantly. Occasionally, the attacks were accompanied by nausea and vomiting. There had been no hemoptysis, bloody or frothy stools. Alkalis afforded some relief. He denied heavy alcohol intake, admitting to one pint of whiskey a month and some small amount of beer. Greasy or rough food seemed to bring on attacks. He had lost 30 pounds in weight in 2 years.

He was examined in the Out Patient Department of The Johns Hopkins Hospital in November, 1952, at which time an epigastric mass was felt. It was believed then that he was suffering either from pancreatic cancer or chronic pancreatitis. He failed to keep a follow-up appointment.

Physical examination, on admission to the Baltimore City Hospitals, in January, 1954, showed a well developed, poorly nourished, Negro of 41 years in no distress. The initial blood pressure was 220/110. The heart was not enlarged. A tender pulsating mass 4 cm. in diameter could be felt in the midline of the abdomen just above the umbilicus. The liver and spleen were not enlarged. X-ray of the abdomen showed multiple calcified areas throughout the pancreas. The urine showed a few white blood cells and 2 plus albumin. Blood counts were normal. Hemoglobin 11.5 gm. Stools were well formed, not bulky, showed no undigested food and no blood. Serum amylase on three occasions was 178, 183 and 88 mg. per cent. van den Bergh 1.0. Thymol turbidity 1.4. Alkaline phosphatase 0.8. Blood sugar 106. X-ray of the gastrointestinal tract showed a deformity of the antrum of the stomach and the first portion of the duodenum from pressure by a smooth mass about 5 cm. in diameter pushing upward from below.

Preoperative impression was chronic pancreatitis with pseudocyst, or carcinoma of the pancreas; and cardiovascular hypertensive disease.

The diagnosis in these two cases was not difficult to make even before operation. Both suffered severe attacks of epigastric pain. One had frothy, fatty stools. The other had a tender epigastric mass. Both showed calcium deposits diffusely spread throughout the pancreas.

Next came the selection of an appropriate operative procedure to relieve these repeated attacks of severe pain from a list of operations that have been recommended for this condition.

1. *Mandatory Procedures:*—a. *Removal of stones from biliary tract:*—An undisputed operative procedure would be to remove stones, if present, from the gallbladder and common duct, and to remove a diseased gallbladder if present. Actually no such condition existed in either patient. If stones are found in either the gallbladder or the common duct, one of these structures should be drained for a period of 6 months or more, in order to divert the pressure of biliary flow from the pancreas.

b. *Relief of jaundice:*—Another undisputed operative procedure would be to relieve obstructive jaundice if present by some surgical means. In neither of our cases was there clinical evidence of jaundice.

2. *Selective Procedures:*—a. *Operations on the sympathetic nerves:*—Actually, the referring physician had sent the first patient to us for this procedure in order to relieve the patient's pain. This operation, however, can be done thoroughly only through the chest. No examination of the pathological condition in the abdomen is possible without a large secondary incision. Moreover, we have not been enthusiastic about this solution to the problem, first of all, because of the reason stated above, and because it does nothing to correct the actual disease of the pancreas. We have employed it with success where the common duct on direct examination at operation is found not to be enlarged.

In the reports from the medical literature unilateral or bilateral splanchnic nerve resections, with or without a concomitant sympathetic nerve resection, and with or without vagectomy, or vagectomy alone, as reported by various authors, although successful in isolated cases, give little cause for enthusiasm for this approach to the problem[14-21]. Such a procedure would have proved entirely wrong in these two patients, as will be explained when the findings at operation are revealed.

3. *Gastric resection:*—Such a procedure has been recommended on the theoretical grounds that diversion of hydrochloric acid from the region of the papilla of Vater will decrease the tendency to spasm of the sphincter and that the absence of food and hydrochloric acid from the duodenum will diminish pancreatic secretion by limiting the formation of secretin[22,23]. Vagectomy has been combined with resection in some cases. This indirect approach has met with varied results. It would not have been a suitable operation in our cases, as will be seen.

4. *Pancreaticolithotomy:*—This procedure has no real place in most cases of pancreaticolithiasis. In occasional instances, improvement following the removal of a solitary stone from the terminal portion of the duct of Wirsung has been observed.

5. *Resection of the pancreas:*—Resection of the distal segment of the pancreas has been undertaken when the pathologic process is confined to the body and tail of the pancreas. Total pancreatectomy has at times been employed[21,24-26] but of course is a very extensive procedure carrying a considerable mortality risk, and carries the additional disadvantage of rendering the patient diabetic.

6. *Anastomosis of the duct of Wirsung* to the upper jejunum, with or without removal of the head of the pancreas and the adjacent duodenum, has been recommended[21] as a reasonable method of management in certain cases. The transection of the duct with anastomosis to the jejunum can be performed in patients in whom the main pancreatic duct is obstructed while the combined transection of the duct and resection of the pancreas, are recommended when the duct of Wirsung is obstructed in its periampullary portion. All are operations which carry quite high morbidity and mortality risks. Nevertheless, if blockage within the pancreatic duct or ducts themselves is responsible for some cases of pancreatitis, the principle of re-establishing drainage of these ducts into the intestine merits further study.

7. *Sphincterotomy:*—Division of the sphincter of Oddi muscle, preferably through a transduodenal approach, with a probe led down through an incision in the common duct, is, of course, based on the premise that abnormal spasm at this sphincter causes interference with normal drainage of bile and pancreatic juice with inflammation of the pancreas resulting[6-8]. It seems logical to employ this procedure when the disease process has not extended so far as to cause dilatation of the common duct and or fibrosis or calcification in the head of the pancreas. Then the obstruction is much more likely due to narrowing of the pancreatic portion of the common duct than to spasm of the sphincter. Any division of this sphincter muscle should be accompanied by drainage of the common duct for several months, depending on the degree of the involvement of the pancreas found at operation.

8. *Choledochojejunostomy Roux-en-Y* is a development of the old cholecystgastrostomy or cholecystduodenostomy. Both these former procedures were followed by an appreciable incidence of reflux cholangitis. Both failed to divert the biliary flow from the opening of the pancreatic duct.

In 1945 Peterson and Cole[27] discussed the occurrence of complete stenosis of the pancreatic portion of the common bile duct following chronic, sclerosing pancreatitis. They described three patients with this disease, all of them jaundiced and recommended a complete division of the common bile duct with

transplantation of its proximal end into an isolated arm of jejunum after the Roux principle.

Bowers[28] went a step further by recommending the operation not only for chronic pancreatitis with a permanently stenosed common bile duct but also for chronic pancreatitis in which the common duct was patent and of normal size throughout. This operation appealed to us because one of us (Trimble) transplanted the common duct successfully into the jejunum in the first one-stage operation ever described for carcinoma of the head of the pancreas[29].

Our preference is to use it for the more advanced cases of chronic pancreatitis, as described in Paragraph 8 above. It was used in the two patients here presented, and served to relieve all pain, to short circuit the bile around a strictured pancreatic portion of the common duct, and to divert the flow of bile completely away from the pancreatic ducts.

Operations employed in the cases cited:—In spite of the fact that the first patient was referred to us for splanchnicectomy, I thought it important in planning his operation, to see directly the region of the pancreas, so decided to perform an exploratory lapraotomy and open the abdomen through a right paramedian incision, which was done on 19 February 1953. The gallbladder was slightly thickened and perhaps, a trifle dilated. The common duct was greatly dilated and hypertrophied. No stones in gallbladder or common duct. The pancreas was very firm throughout and contained many stones. The common duct was opened and we were able to pass a probe only after considerable difficulty through the pancreatic portion of this duct into the duodenum. The duodenum was then opened and the sphincter of Oddi muscle cut directly through on the probe. Even then the dilatation of the pancreatic portion of the duct was not entirely satisfactory.

We debated then whether to transplant the common duct directly into the duodenum or jejunum or, merely to leave a T tube in the undivided common duct, in the expectation that drainage of bile through the T tube and through the cut sphincter of Oddi would allow the pancreas to heal sufficiently to permit a normal flow of bile. We decided on this latter course, closed the duodenum, placed a T tube in the common bile duct, and removed the gallbladder. This organ was removed because it has been said that in these cases concentrated bile in the gallbladder is expressed against the opening of the pancreatic duct, and is a factor in producing the recurring pancreatitis.

As soon as the patient awakened from the anesthetic he stated that all his old pancreatic-type pain was gone, and it did not return. It is most interesting that mere drainage of the common duct relieved this pain entirely. He continued, however, to drain an average of 600 c.c. of bile each day through his T tube. His stools were for the most part acholic and x-rays of his biliary tract with dye introduced through the T tube showed no dye in the duodenum.

Accordingly on 6 May 1953, 3 months later, he re-entered the hospital and the common duct was divided in its suprapancreatic portion and transplanted into the jejunum in a Roux-en-Y fashion. This method diverted the flow of bile completely away from the opening of the pancreatic duct. The patient gained 17½ pounds in the next month and has remained well ever since, now 18 months. He still has some frothy, fatty stools because of the old damage to his pancreas.

At operation on the second patient on 11 February 1954, the pancreas was found to be two or three times its normal size, enlarged throughout, hard and nodular. The head was pressing on the antrum of the stomach and the first portion of the duodenum. The gallbladder was not dilated and contained no stones. No contiguous lymph nodes about the pancreas were enlarged. The common duct was twice its normal size and contained no palpable stones. There was no evidence of any other abnormality within the abdomen.

It was decided that the patient was suffering from chronic pancreatitis. Since the common duct was dilated it was evident that there was resistance to flow of bile either at the ampulla of Vater or in the pancreatic portion of the common duct. There was, therefore, a condition present which might allow bile to flow up into the pancreatic duct or ducts.

Accordingly, a decision was made to transplant the common duct completely and so remove all biliary flow from the pancreatic duct opening. The common duct was isolated from the hepatic artery and the portal vein, and was divided in its suprapancreatic portion. Its distal end was closed with transfixion sutures of silk. The proximal end was temporarily clamped. The jejunum was divided 18 inches below Treitz' ligament. The proximal end of the common duct was then transplanted into the distal end of the divided jejunum and the proximal end of the divided jejunum was implanted into the side of the jejunum distal to this line of anastomosis.

In the intervening 9 months, the patient has gained 10 pounds, has returned to work 8 hours a day as a shipping clerk and has had no pain or other symptoms referable to his abdomen. His stools have remained well formed. X-ray of his gastrointestinal tract, done 4 months postoperatively, shows disappearance of the deformity of the antrum and duodenum and passage of the small piece of rubber catheter which was temporarily placed through the choledochojejunal anastomosis.

In summation, therefore, at operation the findings were much the same in the two cases. Both showed greatly dilated common bile ducts with normal appearing gallbladders and no gallstones. Both had stones throughout the pancreas. One had a localized mass in the pancreas. In retrospect, in the first case it would have been better judgment to have transplanted the common duct immediately instead of merely dividing the sphincter of Oddi. The resist-

ance to biliary and pancreatic flow was due more to the scarring in the pancreatic portion of the common duct than to spasm at the sphincter of Oddi, and was relieved only when the common duct was transplanted 3 months later.

Conclusion:—The present methods of surgical treatment of relapsing pancreatitis are briefly outlined. No single surgical procedure is satisfactory for every case.

Two patients are presented with extensive pancreaticolithiasis, recurring attacks of severe pain, essentially normal gallbladders, greatly dilated common ducts. They were completely relieved of symptoms and restored to health and duty following division and transplantation of the common duct into the jejunum after the Roux-en-Y method.

A finding of great interest to us in these and other cases of chronic pancreatitis is the immediate relief of pain following release of pressure in the biliary tract by drainage of the common duct, either externally by a rubber catheter, or internally by a short-circuiting anastomosis of the biliary system and the intestine around the opening of the pancreatic duct or ducts.

Such findings imply more than the apparent wisdom in recommending this common duct transplantation in certain cases of chronic pancreatitis. They support the old, and now frequently neglected, procedure of draining or diverting the biliary flow in cases of acute as well as chronic pancreatitis. They support the argument that the common duct should be drained and not closed following its instrumentation for removal of stones or relief of stricture, particularly when this instrumentation takes place about the ampulla of Vater, because some degree of pancreatitis is common after such procedures. The transplantation of the common duct offers a reasonable chance for the recovery or prevention of further damage in a diseased pancreas.

Finally, in the surgical treatment of recurring pancreatitis, we are at the present time led to the decision that the region of the gallbladder, common duct, head of the pancreas, and duodenal ampulla should be explored. If any biliary tract disease, such as cholelithiasis or choledocholithiasis, is found it should be corrected surgically, of course. The presence of a diffusely firm pancreas or pancreaticolithiasis, with or without jaundice, calls for additional surgery.

Then the two procedures at the present time best designed to correct the trouble are:

1. In the presence of an *undilated common duct* the sphincter of Oddi should be cut, through a transduodenal approach on a probe passed down the common duct from above. Free passage of graduated dilators down the common duct must be established. The common duct should be drained for several months, postoperatively.

2. In the presence of a *dilated and or* a *hypertrophied common* duct, the evidence is that the obstruction is in the pancreatic portion of the common duct and not at the sphincter of Oddi. Therefore, transection of the common duct and its transplantation into the jejunum in the Roux-en-Y method is indicated.

REFERENCES

1. Körte, W.: Die Chirurgischen Krankheiten und die Verletzungen des Pancreas, Stuttgart, F. Enkey, 1899.
2. Lancereaux, E.: Traite des Maladies du Foie et du Pancreas, Paris, O. Doin, 1899.
3. Opie, E. L.: The Etiology of Acute Hemorrhagic Pancreatitis. Bull. Johns Hopkins Hosp., **12**:182, 1901.
4. Nordmann, O.: Experimente und klinische Betrachtungen uber die Zusammengange zwischen acuter Pankreatis und Erkrankungen der Gallenblase, Arch. f. klin. Chir. **102**:66, 1913.
5. Luim, R. and Maddock, S.: Etiology of Acute Pancreatitis: An Experimental Study. Surgery, **24**:593, 1948.
6. Archibald, E.: The Experimental Production of Pancreatitis in Animals as a result of the Resistance of the Common Duct Sphincter. Surg., Gynec. & Obst., **86**:295, 1919.
7. Archibald, E. and Lewis, D.: Practice of Surgery, Hagerstown, Md., W. F. Prior Co., Inc., 1933, vol. 7, p.l.
8. Doubillet, H. and Mulholland, J. R.: Results of Sphincterotomy in Pancreatitis. J. Mt. Sinai Hosp., **17**:458, 1951.
9. Rich, A. R. and Duff, G. L.: Experimental and Pathological Studies on the Pathogenesis of Acute Hemorrhagic Pancreatitis. Bull. Johns Hopkins Hosp., **51**:212, 1936.
10. Reinhoff, W. F., Jr. and Pickrell, K. L.: Pancreatitis, An Anatomic Study of the Pancreatic and Extrahepatic Biliary Systems. Arch. Surg., **51**:205, 1945.
11. Hicken, N. F. and McAllister, A. J.: Is the Reflux of Bile Into the Pancreatic Ducts a Normal or Abnormal Physiologic Process? Am. J. Surg. **83**:781, 1952.
12. Machella, T. E.: Acute and Chronic Pancreatitis. Veterans Administration Technical Bulletin (TB 10-87), 1953.
13. Veghelyi, P. V.: Secondary Pancreatitis, Am. J. Dis. Child., **74**:1, 1947.
14. Smithwick, R. H.: Discussion, Ann. Surg. **124**:1006, 1946.
15. Fontaine, R., Forster, E. and Stefanini, C.: Resultats eloignes de 63 splanchnicectomies pour diverses affections (en dehors de l'hypertension arterielle chronique permanente), Lyon chir. **41**:279, 1946.
16. Grimson, K. S., Hesser, F. H. and Kitchin, W.W.: Early Clinical Results of Transabdominal Celiac and Superior Ganglionectomy, Vagotomy, or Transthoracic Splanchnicectomy in Patients with Chronic Abdominal Visceral Pain, Surgery, **22**:230, 1947.
17. Reinhoff, W. F., Jr. and Baker, B. M.: Pancreolithiasis and Chronic Pancreatitis: Preliminary Report of a Case of Apparently Successful Treatment by Transthoracic Sympathectomy and Vagotomy, J.A.M.A. **134**:30, 1947.
18. Ray, B. S. and Console, A. D.: Relief of Pain in Chronic (Calcareous) Pancreatitis by Sympathectomy. Surg. Gynec. & Obst. **89**:1, 1949.
19. de Takats, G., Walter, L. E. and Lasner, J.: Splanchnic Nerve Section for Pancreatic Pain. Ann. Surg. **131**:44, 1950.
20. Connolly, J. E. and Richards, V.: Bilateral Splanchnicectomy and Lumbodorsal Sympathectomy for Chronic Relapsing Pancreatitis. Ann. Surg. **131**:58, 1950.
21. Cattell, R. B. and Warren, K. W.: Choice of Therapeutic Measures in the Management of Chronic Relapsing Pancreatitis and Pancreatolithiasis, Gastroenterology **20**:1, 1952.
22. Johnson, W. M.: Subtotal Gastrectomy in the Treatment of Chronic Recurrent Pancreatitis. Gastroenterology **14**:590, 1950.
23. Richman, A. and Colp, R.: Chronic Relapsing Pancreatitis: Treatment by Subtotal Gastrectomy and Vagotomy. Ann. Surg. **131**:145, 1950.
24. Whipple, A. O.: Radical Surgery for Certain Cases of Pancreatic Fibrosis Associated with Calcareous Deposits. Ann. Surg. **124**:991, 1946.

25. Waugh, J. M., Dixon, C. E., Clagett, T. and Bollman, J. L.: Total Pancreatectomy: A Symposium Presenting Four Successful Cases and Report on Metabolic Observations. Proc. Staff Meet., Mayo Clinic, **21**:25, 1946.
26. Rhoads, J. E., Howard, J. M. and Moss, H. N.: Symposium on Recent Advances in Surgical Physiology: Clinical Experiences with Surgical Lesions of the Pancreas. S. Clin. North America, **29**:1801, 1949.
27. Peterson, L. W. and Cole, W. H.: Chronic Sclerosing Pancreatitis Causing Complete Stenosis of the Common Bile Duct. Arch. Surg. **51**:15, 1945.
28. Bowers, R. F. and Greenfield, J.: Choledochjejunostomy: Its Role in the Treatment of Pancreatitis. Ann. Surg. **134**:99, 1951.
29. Trimble, I. R., Parsons, John W. and Sherman, Claude P.: A One-Stage Operation for the Cure of Carcinoma of the Ampulla of Vater and of the Head of the Pancreas. Surg. Gynec. & Obst. **73**:711-722 (Nov.), 1941.

A CLINICAL EVALUATION OF ELORINE SULFATE

I. RICHARD SCHWARTZ, M.D., F.A.C.P., F.A.C.G.*

E. LEHMAN, M.D., F.A.C.G.

J. M. SEIBEL, M.D.

L. GOLDSON, M.D.

W. MANDEL, M.D.

B. J. ROSENTHAL, M.D.

and

P. WEIL, M.D.

Brooklyn, N. Y.

Elorine,† one of the newer anticholinergic drugs has been intensively investigated by us for the past 18 months. Chemically, Elorine is a quaternary ammonium compound with the formula 1-cyclohexyl-1-phenyl-3-pyrrolidino-1-propanol methsulfate. Animal studies[1] revealed effective inhibition of isolated intestinal segments of guinea pig ileum stimulated by methacholine, and marked antispasmodic action on the gastrointestinal tracts of trained and anesthetized Thiry fistula dogs. Pharmacological studies also indicated that there is impressive inhibition of salivary, gastric and pancreatic secretions. Its toxicity is about equal to atropine when given by mouth, but intravenously, Elorine appears to be more toxic than atropine sulfate.

Kirsner and Palmer[2] reported the production of complete anacidity in only one of 11 patients after the intragastric administration of Elorine in doses varying from 25 to 175 mg., the effect lasting for 75 minutes. The volume output of acid was decreased appreciably in several instances. They also reported that mild to moderate side-effects developed in 10 of their 13 patients. Shutkin[3] administered Elorine in doses of 50-100 mg. every 6 hours to 30 cases of peptic ulcer which were observed for 8 months. He found satisfactory clinical responses in 65.6 per cent of his duodenal ulcer patients and noted an incidence of toxic effects in about 24 per cent of those studied.

The purpose of our clinical investigation of Elorine and Co-Elorine‡ was to determine: (1) its efficacy in the treatment of peptic ulcer and other gastrointestinal conditions; (2) its effect on gastric secretion when given orally or by intramuscular injections; (3) its effect on gastrointestinal motility (which will be reported separately at a later date) and (4) the incidence of toxic effects during its use.

From the Gastrointestinal Clinic and Medical Services (Open Division) Kings County Hospital, Brooklyn, N. Y.

*Chief, Gastrointestinal Clinic and Attending-in-Medicine, Kings County Hospital.

†Elorine was liberally supplied by Dr. J. B. Hammond of Eli Lilly & Co.

‡Co-Elorine is Elorine sulfate 25 mg. plus Amytal 8 mg.

Methods

One hundred and sixty-seven patients with varying gastrointestinal complaints have been studied during the past 18 months, 144 of which have been followed long enough to evaluate properly.

In the group we studied were 116 cases of peptic ulcer, 102 duodenal, 9 gastric, and 5 combined. One case of duodenal ulcer was associated with

TABLE I

Diagnosis	No. of Cases	Complete Relief				Significant Relief		No Relief		Stopped because of side-effects	Lost to Follow-up
		in 1 wk. or less		in 1 wk. or more		Severity		Severity			
		3+ 4+	1+ 2+	3+ 4+	1+ 2+	3+ 4+	1+ 2+	3+ 4+	1+ 2+		
Duodenal Ulcer	102	20	26	5	8	9	12	2	7	2	10
Gastric Ulcer	9	1	3				2		1		2
Duodenal and Gastric Ulcer	5	1	1			1	1		1		
Dumping Syndrome	6		1			1		3	1		
Psychoneurosis with G.I. Symptoms	7	1	1			1	1	1	1		1
Diarrhea											
1) Functional	3		1				1				1
2) Ulc. Colitis	1						1				
3) Irritable Colon	1		1								
Duodenitis											
1) Hyepermotility	2	1				1					
2) Chr. Pancreatitis	1		1								
3) Chr. Gallbladder	1					1					
Postcholecystectomy Syndrome	2				1		1				
Ileostomy with Colectomy	1							1			
Cirrhosis of Liver	1										1
Cardiospasm	1										1
G.I. Hemorrhage	1						1				

chronic pancreatitis and another with a posterior gastroenterostomy. There were also three cases of functional diarrhea, 6 cases of dumping syndrome, one case of ulcerative colitis, and 19 cases which fell into a miscellaneous group or were psychoneurotic with hypercholinergic gastrointestinal symptoms (Table I). All the diagnoses were confirmed after complete roentgenological investigations. Most of the patients have been under constant weekly or bi-weekly observation

in our clinic. Histories and physical examinations, blood counts, stools, urines and related chemistries were done in order to determine the presence of toxic reactions to the drug. Several of our patients discontinued the drug because of failure to provide relief from symptoms or because of unpleasant side-effects, but, in no instance were any toxic effects noted relative to blood, liver or kidney functions.

Our patients with peptic ulcer were maintained on the usual bland diet and were also allowed to continue the use of antacids, if the latter had previously been part of their regimen. As was found in our investigations with another anticholinergic drug[4] antacids are frequently necessary in the control of heartburn which at times appears to be uninfluenced by the anticholinergic drugs. We have not followed our patients long enough to make any predictions as to the recurrence rate of peptic ulcer while on this therapy. Only continued investigations for several years can help to form a definitive conclusion about its efficacy in this regard.

Secretion Studies

Two preparations of Elorine were made available for secretion studies, the sulfate salt, which was given orally, and the chloride salt, which was administered parenterally. Only the sulfate salt was used therapeutically.

Gastric secretion studies have been done on 30 cases of proved chronic duodenal ulcer. At the beginning of our investigations we used doses of Elorine sulfate, which were less than 100 mg., in 16 cases and found that the effect on gastric secretion was quite indecisive. In 14 other cases doses of 150 mg. of Elorine sulfate were administered intragastrically and a distinct response in secretory activity was elicited.

A Levin tube was passed after a 12 to 18 hour fast and positioned by trial suction and/or fluoroscopy. Continuous suction was applied by hand syringe or suction pump (minus 3 mm. Hg. pressure) and 20 minute collections made. Basal secretions were determined for one hour to form a base line and then the oral dose of Elorine sulfate was dissolved in a minimal amount of water and injected into the tube. Suction was discontinued for one hour to permit absorption and then re-instituted for another two hours with samples being collected every twenty minutes. Volume was measured and free acid determined by titration with N/10 NaOH using Topfers reagent as the indicator. The effect of intramuscular injection of 25-50 mg. of Elorine chloride on gastric secretion was also determined in 3 additional cases (Fig. 1).

Volume of Gastric Secretion

Eight cases showed a decrease of 50 per cent or more in volume of secretion after intragastric installation of 150 mg. of Elorine sulfate. Two cases

showed a decrease of 45 per cent while 4 cases had decrease of only 20 per cent or less. After intramuscular injection of 50 mg. of Elorine chloride all 3 cases showed greater than 50 per cent decrease in volume of secretion.

Free Acid

After the intragastric administration of 150 mg. of Elorine sulfate 7 cases showed a diminution of free acid of 50 per cent or more. Four cases showed a 45 per cent decrease; one case a 25 per cent decrease, while 2 cases showed

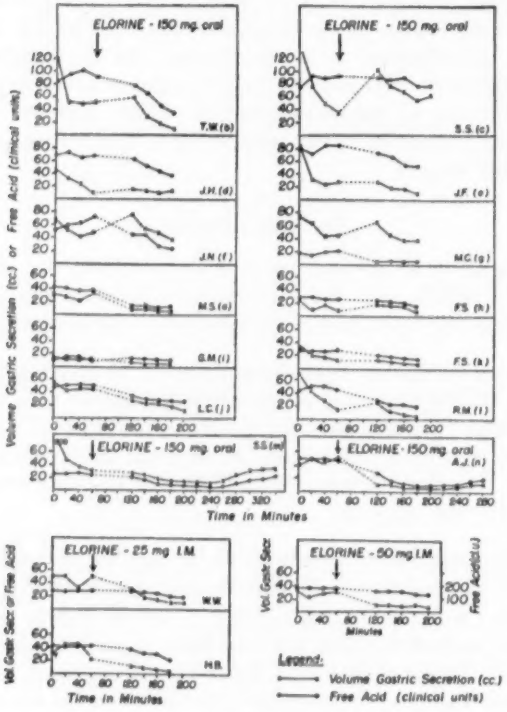
ELORINE - 150 mg. oral
ELORINE - 25 mg. I.M.
ELORINE - 50 mg. I.M.
Volume Gastric Secretion (cc.) or Free Acid (clinical units)
Time in Minutes
Legend:
Volume Gastric Secretion (cc.)
Free Acid (clinical units)

Fig. 1

only 15 per cent or less decrease. After the intramuscular injection of 25-50 mg. of Elorine chloride 2 cases had greater than 50 per cent decrease of free acid concentration and 1 case a mild decrease in free acid.

Clinical Results

Peptic Ulcer:—As will be noted in Table I, we divided our 116 cases of ulcer according to the severity of their symptoms and the amount of relief

obtained after taking Elorine. The dose of Elorine used in most instances was 50 mg. q.i.d In more severe cases 75-100 mg. q.i.d. were given. Of the 39 cases of ulcer suffering from "severe" symptoms, 22 obtained "complete" relief in one week or less; 5 in longer than one week. Ten cases obtained "significant" relief, while two were not relieved at all. In 62 cases with "moderately severe" symptoms, 30 were completely relieved in less than one week, 8 obtained complete relief in longer than one week. In this same group "significant relief" was obtained in 15 cases while 9 cases showed no relief of symptoms at all. Three patients stopped the drug because of annoying side-effects. Success with the drug is manifest when symptoms are ameliorated more rapidly than would be expected with the usual therapy and when there is no recurrence of symptoms while on adequate dosage of Elorine. When complete or significant relief was obtained it was classified as successful therapy. No relief, intolerance to the drug, or recurrence while on adequate dosage was deemed unsuccessful. During the course of treatment 12 patients were lost to our follow-up, bringing the total of ulcers adequately treated to 104. Of these, 77 cases showed success in therapy by prompt and sustained relief of symptoms. Thirteen cases took longer than one would expect such therapy to bring relief and therefore, although they eventually were completely relieved of their symptoms, we are classifying them as unsuccessful therapy because bland diet and ordinary antacids could achieve similar results over the same period of time. Fourteen more patients were considered unsuccessfully treated because they obtained no relief or because they stopped taking Elorine as a result of unpleasant side-effects. In the light of our more recent experience with larger doses of Elorine ranging from 75 to 100 mg. q.i.d., however, we feel that a good number of the above unsuccessfully treated patients could have been salvaged by utilizing a higher dosage at the beginning of therapy.

Dumping Syndrome:—Six patients who complained of symptoms classified as the "dumping syndrome" after subtotal gastrectomy, were treated with doses of Elorine from 50 to 100 mg. q.i.d. One patient obtained complete relief after one week or more while another obtained significant relief. Four patients were not relieved by Elorine. They obtained some relief by utilizing Co-Elorine.

Psychoneurosis:—When strong psychoneurotic symptoms are apparent we feel that Co-Elorine can often bring about an amelioration of symptoms because of its added sedative effect. Seven cases of psychoneurosis with hypercholinergic gastrointestinal manifestations were treated with Elorine and Co-Elorine. Two patients were completely relieved of their symptoms; two obtained significant relief; two were not relieved at all, while one was lost to our follow-up.

Diarrhea:—We have initiated gastrointestinal motility studies by roentgenographic methods and although our studies are not completed, we have sufficient evidence to relate that, in adequate dosage, Elorine has a delaying effect on the emptying time of stomach and small bowel with a lesser effect

on large bowel motility. This will be reported in greater detail at a later date at the end of our motility studies. Three cases of functional diarrhea were treated with 50 mg. of Elorine q.i.d. One patient experienced complete relief, one had signficant relief, while the last patient was lost to our follow-up. One case of ulcerative colitis was given 100 mg. of Elorine q.i.d. and obtained significant relief, but our follow-up period is too short to make any further comment. One case of irritable colon with symptoms of alternating diarrhea and constipation received significant relief from 50 mg. of Elorine q.i.d.

Duodenitis:—Four cases of "duodenitis" two of which were associated with gallbladder disease, one with chronic pancreatitis and the last with hypermotility of the gastrointestinal tract were given Elorine in doses varying from

TABLE II

Side-effects	No. of Cases
None	50
Dryness of mouth	55
Blurring of vision	36
Constipation	11
Urinary obstruction	1
Urinary frequency	6
Heartburn	8
Headache	7
Dizziness	3
Palpitation	3
Drowsiness	2
Nervousness	1
Nausea	1
Asthma	1
Allergic edema of uvula	1

50 to 100 mg. q.i.d. Two cases obtained complete relief of symptoms while the other two were significantly relieved. Their period of follow-up was also too short to reach a more definite conclusion as to the efficacy of this drug.

Elorine and Co-Elorine were also used in a variety of miscellaneous diseases to determine the presence of side-effects, as will be noted by a glance at Table I.

Side-Effects

At the beginning of our investigation we were cautious about increasing our dosage in order to prevent any side reactions. We treated a number of patients with moderately severe symptoms with 25 mg. of Elorine q.i.d. but soon found that this was inadequate in most instances and rapidly substituted

50 mg. q.i.d. as the average dose. In patients with severe symptoms, however, we found that doses of 75 to 100 mg. q.i.d. were absolutely necessary, and in one instance we used 150 mg. q.i.d. (Since our studies were initiated, the manufacturer has increased the recommended dosage to 50-150 mg.) Only when doses of 100 mg. q.i.d. or more were given did side-effects become of such degree as to warrant inclusion in our tabulations (Table II). As with other studies we have made[4], we have been impressed with the fact that side-effects are experienced more often and to a greater degree by highly emotional and highly susceptible individuals. Dryness of the mouth was complained of most often, as would be expected, but in only 35 per cent of the total number of cases. Blurring of vision was noted in only 24 per cent of our patients and was disturbing to none. We found 7 cases of urinary difficulties, with slowing of the stream in one case and with complaint of frequency of urination in 6. We feel that the latter side-effect is due to the greater amount of water or milk which is taken to overcome the dryness of the mouth so frequently experienced. Constipation was found in only 11 per cent of our patients, all of whom responded readily to milk of magnesia. Surprisingly enough, quite a few patients stated that while on Elorine their bowel movements became more regular than without the drug. Heartburn was a minor complaint, being found in only 5 per cent of the patients, and responding to the usual antacids. Only 2 per cent or less of patients complained of drowsiness, dizziness, palpitation or headache. Thirty-four per cent of the patients had no complaints whatsoever.

Complications

During treatment three patients developed melena while four showed evidence of postpyloric obstruction. All seven of these patients were eventually operated upon and fell into the "no-result" group. One patient had to terminate treatment because of the onset of an acute myocardial infarction. Five patients discontinued treatment because of annoying side-effects.

During the 18 months of follow-up on our ulcer patients, 19 cases or about 16 per cent, developed recurrence of symptoms while under treatment. Most of them responded to larger doses of the drug but two patients could not be relieved at all and required a change in medication in order to bring amelioration of their symptoms.

Summary and Conclusions

Elorine, a new anticholinergic drug, has been investigated in the treatment of 167 patients with hypercholinergic gastrointestinal manifestations.

Our largest and most significant group was 104 cases of peptic ulcer. A much smaller group of cases with dumping syndrome, functional diarrhea,

irritable colon, ulcerative colitis, duodenitis and gastrointestinal neurotics were also treated.

Seventy-seven cases, or 74 per cent of our 104 ulcer cases were classified as successfully treated. In the light of our increased experience with the drug we believe a greater percentage could have been helped by employing doses larger than the initially recommended 50 mg. q.i.d.

Twenty-two cases in the miscellaneous hypercholinergic group showed 73 per cent of successful therapy, although the number of cases in each category is not satistically significant.

Gastric secretion studies revealed a distinct response in diminution of volume and free acidity only when the dose intragastrically was 100 mg. or more.

Side-effects have been surprisingly moderate in number and severity. Only five patients could not tolerate the drug because of toxic effects (a total of 3.4 per cent).

Although the average dosage has been established as 50 mg. q.i.d. we feel that in many instances 75 and even 100 mg. q.i.d. can be taken with impunity and will bring much more successful results. The larger doses are certainly necessary for therapeutic purposes while the dose of 50 mg. q.i.d. can be used as a maintenance dose.

Elorine and Co-Elorine are valuable additions to the present day treatment of diseases manifested by hypercholinergic symptoms.

REFERENCES

1. Lee, L. M., Gibson, W. Dinwiddie, W. G. and Mills, J.: The Pharmacology of Compound 14045, from the Lilly Research Laboratories, Eli Lilly and Co. to be published.
2. Kirsner, J. B. and Palmer, W. L.: Newer Gastric Antisecretory Compounds, J.A.M.A. **151**:798-805 (Mar. 7), 1953.
3. Shutkin, M. W.: The Medical Treatment of Peptic Ulcer with a New Anticholinergic Compound, Am. J. Gastroenterol., **21**:386-392 (May), 1954.
4. Schwartz, I. R., Lehman, E., Ostrove, R., and Seibel, J. M.: A Clinical Evaluation of a New Anticholinergic Drug, Gastroenterology, **25**:416-429 (Nov.), 1953.

President's Message

We are a comparatively new organization, unique in a way, because we include several medical specialties aiming at a common goal. The gradual change from the old to the new has been exceptionally well planned and executed and now needs to be perfected. Our College must be improved, our policies defined, and responsible personnel brought to the foreground. Organization is sometimes mentioned as the wedding of authority and responsibility because, in its essentials, it consists of assigning specific functions to designated people or departments, with authority for them to be carried out plus accountability to management for the results obtained.

"What are we aiming at?" is the beginning of wisdom in organizational planning. Are we interested in the best possible care for the gastroenterological patient? Do we want to take it to the general practitioner in the form of the printed word, seminars, group discussions, etc.? Do we want to improve our own membership and influence gastroenterologically minded physicians and surgeons in allied fields? Do we want to urge the creation of departments in medical schools and hospitals? How do we proceed?

We must define policies in order that continuity and consistency of effort result. It is hoped that the medical profession at large becomes cognizant of our hopes and aspirations and that those interested join our ranks. Many fine men are in the field today and much talent is available both in and outside our group.

We must insure the execution of accepted policies and plans by maintaining a headquarters staff of painstaking trained people, professionals in their field. These individuals are charged with the carrying out of the details in a dignified and creditable fashion.

At this point coordination of committees and departments becomes imperative. Each detail can be evaluated and emphasized or subordinated according to its merit.

This is the function of our headquarters staff, and they need our help and unbiased suggestions in order to properly carry out a good balanced plan. A give and take philosophy in the hands of many, with authority vested in few, will bring success to our College.

Lyon A. Ferguson

ABSTRACTS FOR GASTROENTEROLOGISTS

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STOMACH

THE NATURE OF GASTRIC HYPERSECRETION OF ACIDS IN PATIENTS WITH DUODENAL ULCER: J. N. Hunt. and A. W. Kay. Brit. M. J. 4902:1444 (Dec. 18), 1954.

The results of an augmented histamine test, consisting of giving large doses of histamine while protecting the patients against the extragastric actions of histamine by previous administration of an antihistaminic, are discussed. Examinations were performed on 27 male subjects without peptic ulcer and 152 male patients with duodenal ulcer who were operated on. Results are expressed in terms of the volume of parietal component formed by the acid-secreting cells. Analysis of the results shows that the maximal secretion and the basal secretion of acid are both greater in the duodenal ulcer group. The percentage of the maximal secretory capacity active during periods of basal secretion is not significantly different in the two groups. The conclusion is reached that the basal hypersecretion of acid in duodenal ulcer may be accounted for by the increased maximal secretory capacity. There seems to be no need to postulate an increase in excitation bearing on the parietal cells in patients with duodenal ulcer during basal secretion.

In ulcer patients who develop stenosis, the raised maximal secretory capacity for acid appears to be due to a work hyperplasia of the parietal cells and increases with increase in duration of symptoms.

ARNOLD L. BERGER

IS TOTAL GASTRECTOMY JUSTIFIED IN CARCINOMA OF THE STOMACH?: Ralph Colp and E. Jemerin. N. Y. State J. Med. 55:75, (Jan. 1), 1955.

The question has been raised as to whether a further improvement in long-term results (three and five-year survival rates) would not be obtained by the more frequent or routine use of total gastrectomy even in early limited lesions.

While the mortality of total gastrectomy has been much reduced, it remains appreciably higher than that for subtotal resection. It is likely that any increase in survival would be outweighed by the greater death rate from the procedure. Moreover, morbidity and invalidism, following total gastrectomy, are significant features. Total gastrectomy does not solve the problem of eradicating lymphatic spread beyond the limits of technical accessibility, and this is the condition responsible for most survival failures. A significant improvement in long-term survival will probably depend upon earlier diagnosis when the lesion is still relatively confined, permitting the performance of a standardized radical subtotal gastric resection. Total gastrectomy should be reserved for those cases in which the entire or proximal stomach is involved.

FRANZ J. LUST

BENIGN ULCERS OF THE GREATER CURVATURE OF THE STOMACH: Charles H. Brown and Anthony D. Intriere. Cleveland Clin. Quart. 22:27 (Jan.), 1955.

The authors have reviewed the literature and add two cases of their own in which there were benign ulcerations along the greater curvature of the pars media of the stomach, and each had multiple gastric ulcers one having two and the other four. Both patients were advised to undergo surgery because of the possibility of malignancy and were proven benign after pathological examination of the lesions.

JACOB A. RIESE

A NEW ANTACID—EVALUATION OF TREVIDAL IN PEPTIC ULCER AND GASTRITIS: J. L. Klauber, A. R. New and P. J. Pagano. Therapeutics. 83:169 (Feb.), 1955.

Trevidal is a new antacid and is a balanced combination of ingredients having clinically established value as antacid plus a unique demulcent gum with optimal viscosity and mucosa-covering qualities even in highly acid gastric juice.

The authors found Trevidal to be the most nearly ideal antacid in a study where they observed 50 patients divided into 3 groups.

Group A:—Thirty-one patients, those having an active duodenal ulcer or gastric ulcer of long standing. These were given 2 tablets before meals, two tablets after meals, two tablets before retiring and two tablets to be taken at any time of day or night that distress occurred. Four patients did not respond at all, 3 were later hospitalized for pyloric obstruction. The results in the remaining 24 cases were very impressive, giving relief of symptoms for prolonged periods, healing of the ulcer and gastroscopic findings showed coating over the irritated mucosa, not obtainable with other antacids. In only several cases was combined therapy used.

Group B:—Nineteen patients suffering from gastritis, acute, atrophic and hypertrophic type. These were instructed to take 2 tablets whenever they had epigastric distress. Results were as good as in group A.

Group C:—Two patients, both with prolapse of gastric mucosa into the duodenum. These were given 2 tablets three times a day and whenever epigastric distress occurred. Both obtained complete relief after 5 days' treatment. It seems that Trevidal provided a protective covering over the protrusion and neutralized the gastric acid thus preventing ulceration from occurring.

No toxic effects were observed in any of these patients.

The author reviews several cases with the history, progress and treatment of each case. The author then concludes that Trevidal is especially suitable for use in general practice, particularly for ambulatory patients.

LOUIS K. MORGANSTEIN

INTESTINES

URETERAL TUMORS AS A CAUSE OF BIZARRE ABDOMINAL SYMPTOMS ILLUSTRATED WITH A SERIES OF CASE STUDIES: William J. Baker and Edwin C. Graf. Am. Pract. & Digest. Treat. 6:25 (Jan.), 1955.

The authors present a timely review of lesions outside the realm of the gastrointestinal tract with gastrointestinal symptoms, ureteral tumors (of which 6 cases are presented), solitary as well as polycystic disease of the kidney, tumors of the kidney, hydro-ureter and hydronephrosis, ureteral calculi and acute vasiculitis may mimic acute or chronic appendicitis or acute and chronic cholecystitis. Rectal pain and pruritus may be caused reflexly by pathology in the genitourinary tract.

In the cases presented the major signs and symptoms were: abdominal pain, abdominal masses, abdominal distention, dyspepsia and ileus. An attempt is made by the authors to explain this on the basis of common origin of the sympathetic nerve supply to the gastrointestinal and genitourinary tracts which lies imbedded in the retroperitoneal tissues.

Irritation of these nerve plexuses can produce symptoms of either gastrointestinal or genitourinary diseases. Thus, patients with gastrointestinal complaints with negative findings deserve a complete survey of the genitourinary tract.

A. J. BRUNNER

LIVER AND BILIARY TRACT

ACUTE CHOLECYSTITIS: W. Burnett. Lancet. 266:488-490, 1954.

The bromsulfalein test is a valuable means of differentiating acute cholecystitis from other gallbladder diseases and from nonbiliary intraperitoneal conditions. The amount of dye retention parallels the degree of inflammation. In contradistinction only 5 of 55 patients with other intraabdominal diseases showed retention of the dye. Regular exhibition of morphine, or of meperidine hydrochloride (demerol), or of amidon occasionally resulted in false positive reactions.

REGINALD B. WEILER

ABDOMINAL AORTOGRAPHY FOR THE ROENTGEN DEMONSTRATION OF THE LIVER AND SPLEEN: L. G. Rigler and P. C. Olfelt. Am. J. Roentgenol., 72:586, (Oct.), 1954.

A procedure for the roentgen visualization of the liver and spleen by means of introducing of a contrast medium through the abdominal aorta is described. A rapid exposure technic with multiple films will permit reasonably adequate demonstration of the size, shape, position and internal structure of the liver and spleen. The hepatic and splenic arteries and the portal venous circulation are sufficiently well demonstrated so that diseases of these structures can be elucidated. Diseases of the liver, itself, especially cirrhosis and metastases from tumors are usually well delineated. Until a contrast medium which is harmless can be introduced into the liver by the oral or intravenous route, the pathway through the abdominal aorta may be the method of choice.

FRANZ J. LUST

ROENTGEN DIAGNOSIS OF GALLBLADDER AND BILIARY TRACT DISEASE WITHOUT CHOLECYSTOGRAPHY: R. L. Scanlan and B. R. Young. Am. J. Roentgenol., 72:639, (Oct.), 1954.

Conventional roentgenograms without the aid of cholecystography often reveal valuable information concerning gallbladder and biliary tract disease. The arrangement and range of movement of stones may be the only indication of a distended gallbladder or duct calculi. An enlarged gallbladder indicating cholecystic or ampullary disease may be of sufficient opacity for detection and the inferior margin is frequently outlined by contiguous gas-filled loops of intestine. Air in the biliary tract indicates abnormal communication with the intestinal tract or infection with gas-forming organisms. Prone, supine or lateral decubitus views have been an invaluable combination far superior to any single projection in the roentgen diagnosis of gallbladder and biliary tract disease without cholecystography.

FRANZ J. LUST

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ACUTE HEPATIC INSUFFICIENCY OF THE CHRONIC ALCOHOLIC: Gerald B. Phillips and Charles S. Davidson. A.M.A. Arch. Int. Med., 94:585, (Oct.), 1954.

Most chronic alcoholics with cirrhosis of the liver improve rapidly with proper conservative therapy. At times, however, cases with an acute hepatic insufficiency are encountered which recover very slowly or even progress to hepatic coma and death in spite of appropriate treatment. Therefore, a group of 18 patients showing such a fatal outcome was investigated at autopsy. All patients had an extremely poor dietary intake for months or even years. Microscopic examination of the liver revealed abnormalities originally described by Mallory consisting of severe parenchymal disorganization with liver cell necrosis and "alcoholic hyalin", an intracellular homogenous substance rarely found in nonalcoholic cirrhosis or in any other liver disease. These pathological changes seem to occur independently from the fibrosis and the fatty infiltration seen in the majority of patients with cirrhosis in whom the disease has a much better prognosis. Therefore, a different etiological basis is suspected for each type of liver cirrhosis and the possibility of a direct effect of the alcohol on the liver cells causing the severe destruction is suggested.

H. B. Eisenstadt

ESOPHAGEAL VARICES IN NON-CIRRHOTIC PATIENTS. ESOPHAGOSCOPIC STUDY: Eddy D. Palmer and Irving B. Brick. Am. J. Med., 17:641, (Nov.), 1954.

Esophageal varices occur in about two-thirds of all patients with hepatic cirrhosis. They are also present in primary and secondary extrahepatic portal vein obstruction. However, they can be found in a variety of other liver diseases. For instance, in chronic passive congestion, associated with heart failure, in visceral schistosomiasis, amebic hepatitis, hepatic hemosiderosis associated with congenital hemolytic jaundice and in acute virus hepatitis. The formation of esophageal varices in the latter disorder is very rapid. They may be visualized by esophagoscopy within one week from the onset of the disease. In congestive heart failure varices differ in as much as they bleed very rarely and they are mostly located in the mid-esophagus in contrast to those occurring in other hepatic disorders which have a considerable tendency to bleed and involve principally the distal segment. No varices have been found in fatty livers and hepatic sarcoidosis.

H. B. Eisenstadt

USE OF VERSENOL IN THE TREATMENT OF HEMOCHROMATOSIS: M. J. Seven, H. Gottlieb, H. Israel, J. G. Reinhold and M. Rubin. Am. J. M. Sc., 17:646-51, 1954.

The authors in a small series found that N-hydroxyethylethylene diamine triacetic acid (Versenol) caused a marked increase of urinary excretion of iron in a patient suffering from hemocrhomatosis. A similar result was found in another patient with evidence of abnormal iron storage in the tissues (questionable hemochromatosis). It was also found that the enhanced iron excretion continued into the posttreatment period. However, in comparison to venesection, considerably less iron is lost in this way—e.g. 265 mg. of iron for a half a liter of blood as compared to 16 mg. with a course of 3 days of Versenol. This method may be useful where phlebotomy is contraindicated. Liver function studies showed that there were no untold effects in the use of this drug.

J. R. Van Dyne

THE FUTURE OF PATIENTS CHOLECYSTECTOMIZED FOR DYSKINESIA OF THE GALLBLADDER: Guy Albot and G. F. Bonnet. Arch. Mal. appar. digest. 43: 785-798 (July), 1954.

This paper is based on the complete study of 27 patients by different surgeons before, during and after operations for hypertonic vesicular dyskinesia. In every case the dyskinesia was accompanied by inflammatory anatomical lesions (cysticitis, diffuse cholecystitis, pericystitis) or dysplasic lesions (adenofibromatosis of the Lyschka-type, strawberry gallbladder), or fibrous lesions of uncertain origin. There was no connection between the histological lesions and pre- and postoperative symptoms.

The delayed action results obtained after cholecystectomy are frankly mediocre. In

only 20 per cent of the cases did painful hepatobiliary attacks disappear. In the other patients, after several months of postoperative relief, pains in the right hypochondrium reappeared.

Two factors seem to play an essential part: migraines and the psychic condition of the patients. In no case were the migraines and their attendant bilious attacks modified by the operation. The mental background of the patients suffering from dyskinesia, made up of passivity, anxiety and hypochondria is aggravated by the operation, in particular in the case of sufferers from migraine. The only good results were observed in those patients whose psychic state was sound.

Finally, gastrointestinal syndromes, existing before the operation and often independent of the biliary trouble, (gastritis, gastroduodenal ulcer, fermenting colitis, spasmodic colitis) occupy an important place in the disorders found in these patients. One should therefore be extremely cautious before subjecting a patient suffering from vesicular dyskinesia to cholecystectomy, even when it is accompanied by infundibulo-cystic lesions proved by cholecystography, duodenal tubage and biliary radiomanometry.

Patients suffering from migraine or presenting characteristic anomalies have little chance of relief. Without as yet being able to prescribe a precise line of therapy, it seems clear that cholecystectomy does not prove, in the majority of cases, to be a satisfactory treatment for biliary dyskinesia.

LIGATURE OF THE COMMON HEPATIC ARTERY IN CIRRHOSIS. MECHANISM OF THE ACTION ACCORDING TO RESULTS OBTAINED IN CASES OF INITIALLY ANASCITIC CIRRHOSIS: Guy Albot and Lucien Leger. Presse Med. 62:1794 (Dec. 25), 1954.

It is customary to restrict ligature of the common hepatic artery to cases of decompensated cirrhosis accompanied by ascites or by hemorrhagic varicosity of the esophagus.

Failure to operate in cases of initially ascitic cirrhoses, which has been a tenet up to the present time, would be unassailable if there was any medical treatment available to interrupt the course of events. In actual fact, such is not the case and sooner or later, these patients reach the stage of decompensation, ascites and death.

The authors report the first attempt at treatment by ligature of the hepatic artery in these incipent cirrhoses. They endeavor to explain exactly in three cases in point the action of the operation and its mechanism.

Contrary to the currently accepted view, these cases reveal that ligature of the hepatic artery does not cause a fall in portal pressure and that preoperative variations in this pressure are due to fluctuations in general arterial pressure, and if such is the case, this operation with its undoubted action upon the development of morbidity must be explained by some other mechanism.

In the 3 cases studied, the ligature did not have any noticable effect on the aggregate protein content of the blood nor that of the albumin and globulins as happens in ascitic forms (a fact with confirms Rienhoff's hypothesis according to which the improvement of proteins in ascitic cirrhosis is due to the drop in the escape of the blood proteins into the ascitic liquid). The regular improvement of the bromosulfanaphthaline and its early results supports the theory that it is the result of accelerated flow of the portal blood. Passage tests (diuresis, lactosis and hippuric acid) have not shown any considerable improvement during the succeeding months, any more than have the Mac Lagan and Kunkel tests. On the other hand, the Rec Colloidal Test carried out with the antigen and according to the technic described by Guy Albot and M. Corteville, gave a definite reaction in 3 cases in which it varied from a strong reaction to a normal one, quite permanently in 2 cases and temporarily in 1. Therefore, the modifications in these functional examinations are undeniable but complicated. Their late appearance would seem to suggest that they are not brought about through the intermediary of a decline in portal pressure, but rather through the fact that they promote regeneration of hepatic parenchyma.

In only one of the three cases did the authors have a sufficient time lapse to compare the histology of the liver before and 26 months after the ligature, with four interim studies. This case enables them to assert that this operation promotes the regeneration of the parenchyma and checks

proliferation of the conjunctive tissue, as the appearance of the liver, sampled either by injection biopsy or by surgical biopsy, proves. This result was a late development and its exceedingly spectacular nature seems due to the fact that the operation was carried out early on a patient with incipient cirrhosis, biologically decompensated, but clinically still latent. This prolonged action is late in manifesting itself and fits in badly with the hypothesis of a decline in the level of portal pressure: it is more compatible with the hypothesis of Chenoweth, Berman and Hull who consider that the operation restores the speed of portal flow and thus promotes regeneration of the hepatic tissue whilst preventing the spread of inflammatory conjunctive lesions.

POSTCHOLECYSTECTOMY ORAL CHOLANGIOGRAPHY: J. Russell Twiss, Lee Gillette, Samuel L. Beranbaum, Maxwell J. Poppel and Eilif C. Hanssen. A.M.A. Arch. Int. Med. 95:59 (Jan.), 1955.

Oral cholangiography may give valuable diagnostic information in a number of patients with nonfunctioning gallbladder or with postcholecystectomy status. The technic is simple and consists of administering a double dose of telepaque (12 tablets) withholding all liquids for twelve hours prior to the x-ray examination to achieve dehydration, and giving two teaspoonsful of paregoric two hours after the dye to induce a sustained spasm of the sphincter of Oddi. Best x-ray pictures were obtained in some patients five hours, in others 12 hours after the telepaque. Dyskinesia was demonstrated by a marked widening of the common duct to 10 mm. and more without signs of obstruction after the administration of amyl nitrate or the ingestion of a fatty meal. Cystic duct remnants, reformed gallbladder, ductal stones and ductal obstruction were also demonstrated in several cases with this method.

H. B. EISENSTADT

DECREASED RED CELL SURVIVAL ASSOCIATED WITH LIVER DISEASE: Philip N. Jones, Irwin M. Weinstein, Richard H. Ettinger and Richard B. Capps. A.M.A. Arch. Int. Med. 95:93 (Jan.), 1955.

An anemia is frequently present in liver diseases especially cirrhosis and it rarely responds to liver extract injections because the bone marrow shows erythroid but not megaloblastic hyperplasia. Hemolysis has been suspected to be the cause of this anemia but an increased fecal urobilinogen has been demonstrated only in a limited number of such cases. At the present the most accurate way of measuring the degree of hemolysis is the determination of the red cell survival time with radioactive sodium chromate. This method shows a decreased red cell survival in practically all cases of hepatic disease with anemia and in many without decrease of the peripheral white cell count. In the latter cases the bone marrow is able to compensate for the increased hemolysis by increasing the output of hemoglobin and red cells. The failure to find an elevation of fecal urobilinogen in all cases cannot be explained properly at this time, but this has been noticed by various investigators. The cause of the increased hemolysis in liver disease might be hypersplenism secondary to portal hypertension. The striking reduction of serum bilirubin in liver diseases after the administration of cortisone and corticotropin might be caused by a change of the hemolytic process rather than an alteration of the liver functions. The high incidence of gallstones observed in chronic liver disorders can at least be partly explained by an increased hemolytic process.

H. B. EISENSTADT

FATE OF THE CHOLECYSTOSTOMY PATIENT: D. M. Hays and F. Glenn. J. Am. Geriatric Soc. 3:21-30, (Jan.), 1955.

Cholecystostomy is a safe, dependable surgical procedure generally reserved for use in patients in whom cholecystectomy is contraindicated. It can only rarely be regarded as definitive therapy, and in most cases, must be followed by elective chole-

cystectomy. It is the operation of choice if life expectancy is less than two years, as in patients with advanced carcinoma, leukemia or cirrhosis with bleeding varices, as death will usually occur from the primary disease before recurrences of further biliary tract disease. If the life expectancy is likely to be over two years (and life expectancy figures are rising), the chances of subsequent biliary tract disease are over 50 per cent. Elective cholecystectomy is then the procedure of choice, either in itself or following an emergency cholecystostomy. Otherwise, there is definite possibility of such patients requiring emergency biliary tract surgical intervention under less than optimal conditions.

ARNOLD L. BERGER

THE DIAGNOSIS AND MANAGEMENT OF BILIARY TRACT DISEASE: Robert M. Zollinger, E. Thomas Boles and Glenn B. Crawford. New England J. Med. 252:203 (Feb. 10), 1955.

The author indicates the complications and uncertainties following biliary tract surgery and attempts to evaluate the management of acute cholecystitis and common duct stones that have proved satisfactory over a period of six years.

The positive demonstration of stone is the ideal basis for surgery. A single demonstration with nonvisualization is an inadequate criterion and should be repeated with an increased dose of dye. In patients with repeated biliary colic, surgery may be advised despite an apparent normal gallbladder, but stones should be recovered in every case of cholecystectomy.

In acute cholecystitis, hospitalization is advised. If the symptoms subside surgery is delayed until the patient is ambulatory. In the authors group, 60 per cent were operated on several days to a week after admission, instead of sending them home to return in several weeks for elective surgery. In 20 per cent of another group they were operated on within 24 hours after admission.

The authors found common duct stones in about 20 per cent of all patients with cholelithiasis. In the author's series pancreatitis was responsible for 50 per cent of the 12 deaths. Common duct stones were removed in 35.5 per cent in all secondary operations on the biliary tract.

Jaundice:—The authors delay surgery if cephalin flocculation and thymol turbidity tests are elevated and if prothrombin time cannot be raised 50 per cent in spite of Vitamin K therapy. If cholesterol esters are below 50 per cent normal or serum-mucoprotein below 40 per cent per 100 c.c., surgery should be postponed. If these tests are within normal range, but alkaline phosphatase is elevated, common duct stone or carcinoma should be considered. The presence of a white stool and existence of jaundice longer than 3-4 weeks is an indication for surgery.

LOUIS K. MORGANSTEIN

PATHOLOGY AND LABORATORY RESEARCH

THE EFFECT OF PROLONGED ADMINISTRATION OF LARGE DOSES OF SODIUM BICARBONATE IN MAN: G. Van Goidenhoven, O. V. Gray, A. V. Price, 2nd and P. H. Sanderson. Clin. Sc., 13:383-401, (Aug.), 1954.

An investigation was conducted relative to the efficacy of constant administration of sodium bicarbonate in milk as a therapy for peptic ulcer. The amount of bicarbonate necessary to maintain a pH 4 or over, of the stomach contents, was sought. In gastric ulcer a daily intake of 20 to 40 grams was sufficient, while in duodenal ulcer as much as 80 to 100 grams was required. Doses up to 140 grams of Na_2CHO_3 daily produced no untoward side-effects. The authors deduce that simple alkalosis rarely causes any renal pathology. Renal failure is usually the result of dehydration and renal ischemia. Severe limitation of available renal bicarbonations results when there is a fluid depletion combined with a fall of the glomerular filtration rate.

REGINALD B. WEILER

DEHYDRATION WITH HYPERNATREMIA, HYPERCHLOREMIA AND AZOTEMIA COMPLICATING NASOGASTRIC TUBE FEEDING: Frank L. Engel and Carl Jaeger. Am. J. Med., 17:196, (Aug.), 1954.

Five cases of dehydration with hypernatremia, hyperchloremia and azotemia, following prolonged tube feeding with a high protein formula, to persons with impaired level of consciousness have been observed. These patients received 170 to 200 grams of protein daily dissolved in 2,000 to 3,600 c.c. of fluid. This amount of water was apparently insufficient for the excretion of all the nitrogen as well as the other solutes and lead to hyperosmolarity of the serum as well as general dehydration with azotemia. Such electrolyte disturbance was clinically associated with a deterioration of the patient's condition. Therefore, a formula for tube feeding containing not more than 75 grams of protein per 2,500 c.c. of water is recommended for routine administration. This dosage is contrasted to a proprietary tube feeding powder recently put on the market with instructions suggesting a concentration of 230 grams of protein per 2,500 c.c. of fluid.

H. B. Eisenstadt

THE LOW CHOLESTEROL, LOW FAT DIET: C. H. Robinson. Am. J. Clin. Nutrit., 2:353-355, (Sept.-Oct.), 1954.

A low cholesterol, low fat diet which provides the recommended dietary allowances for men or women has been described. In the lists of food to avoid, separate categories have been set up for foods high in cholesterol and high in fat. Some foods obviously fall in both groupings. It is possible to modify the diet so that it is low in exogenous cholesterol but contains more liberal allowances of fat, or vice versa. Since the value of this diet in vascular disease has not been established, and since it must be used indefinitely by those patients whom it may benefit, it is essential that the diet not be used indiscriminately. The patients for whom the diet is prescribed should be evaluated at frequent intervals to determine any possible benefits accruing from this regimen.

Arnold L. Berger

DIET AND PLASMA CHOLESTEROL LEVELS: Mayer, Connell, DeWolfe and Beveridge. Am. J. Clin. Nutrit., 2:316-322, (Sept.-Oct.), 1954.

Five apparently healthy male subjects were placed upon diets with varying amounts of cholesterol per day and varying proportions of the total calories in the form of fat, vegetable and/or animal.

The diet low in fat and in cholesterol led to a highly significant decrease in plasma cholesterol levels, whereas the addition of cholesterol in the form of egg yolk did not cause any change. When the proportion of dietary fat was increased in the form of vegetable fat, a signficant increase occurred in plasma cholesterol levels, and these levels were not significantly increased by a substitution of animal fat for the vegetable fat. The results of this investigation indicate that, within the limits studied, dietary cholesterol has no effect on plasma cholesterol levels, whereas alterations in the level of dietary fat, whether of animal or vegetable origin, led to parallel changes in plasma cholesterol.

Arnold L. Berger

BOOK REVIEWS FOR GASTROENTEROLOGISTS

BEYOND THE GERM THEORY—The Roles of Deprivation and Stress in Health and Disease with a foreword by Howard R. Craig, Director, New York Academy of Medicine: Iago Galdston, M. D., Editor. A New York Academy of Medicine Book. 182 pages, graphs and tables. Health Education Council, New York, N. Y., 1954. Price $4.00.

The book is divided into four parts and eleven chapters. The reader will note that the concepts of Claude Bernard, Walter Cannon and Hans Selye may now be successfully applied to the prevention and treatment of disease and the promotion of health.

The authors of these various chapters are well known in their given field and the reader will find many interesting theories and suggestions in coping with individuals or groups.

SURGERY OF THE ADRENAL GLANDS: William Wallace Scott, M.D., Ph.D., Professor of Urology, Johns Hopkins School of Medicine, Director, James Buchanan Brady Urological Institute, Baltimore, Md. and Perry B. Hudson, M.D., Assistant Professor of Urology, Columbia University College of Physicians and Surgeons, etc., New York. 150 pages, illustrated. Charles C. Thomas, Springfield, Ill., 1954. Price $3.50.

Surgery of the Adrenal Glands is a well written and documented monograph of the American Lecture Series which is edited by Dr. Lester R. Dragstedt. It will be found of great value by the urological and abdominal surgeon who may be called upon to diagnose and operate when the adrenals are involved.

CLINICAL APPROACH TO JAUNDICE: Leon Schiff, M.D., Ph.D., Professor of Clinical Medicine, University of Cincinnati College of Medicine, Director of Gastric Laboratory, Cincinnati General Hospital. 113 pages, illustrated. Charles C. Thomas, Springfield, Ill., 1954. Price $3.75.

Dr. Schiff needs no introduction to the medical profession. His book, "The Differential Diagnosis of Jaundice" which appeared in 1946, is a classic and was well received by the profession. In this monograph on "Clinical Approach to Jaundice", Dr. Schiff elaborates and brings up to date the clinical picture, findings and diagnosis in the various types of jaundice.

It is recommended highly, both to the general practitioner and gastroenterologist.

ANNUAL REVIEW OF MEDICINE—VOLUME 5: Windsor C. Cutting, Editor, Henry W. Newman, Assistant Editor, Stanford University School of Medicine. 490 pages. Annual Reviews, Inc., Stanford, Calif., 1954. Price $7.00.

As in previous years, the Annual Review of Medicine covers the entire field of medicine including the specialties. There is an extensive literature index at the end of each subject and an author and cross-index complete the volume.

Physicians who wish to be up to date in the newer diagnostic and therapeutic methods will find this fifth volume a valuable addition to their library.

A STORY OF AMERICAN OPPORTUNITY: Hugh Roy Cullen, Ed Kilman and Theon Wright. 376 pages. Prentice Hall, Inc., New York, N. Y., 1954. Price $4.00.

Mr. Cullen's story reads like a Horatio Alger novel. In this biography, the reader will find that the early life of Mr. Cullen was characterized by courage and integrity. He struck it rich and accumulated close to a billion dollars, giving away most of it to the University of Houston and to Houston hospitals.

It is a worthwhile book and is recommended to be read by young Americans.

A DEVOTION TO NUTRITION: Frederick Hoelzel, Assistant in Physiology, University of Chicago. 88 pages. Vantage Press Inc., New York, N. Y., 1954. Price $2.50.

The author relates his own experience since he was six years of age. It seems that Mr. Hoelzel is a faddist and advocates fasting to improve mental and physical health. His studies in nutrition were greatly influenced by Carlson's interest and publications. Mr. Hoelzel's fasting days amount to about 1,000, of which 41 days and 17 hours were in one stretch.

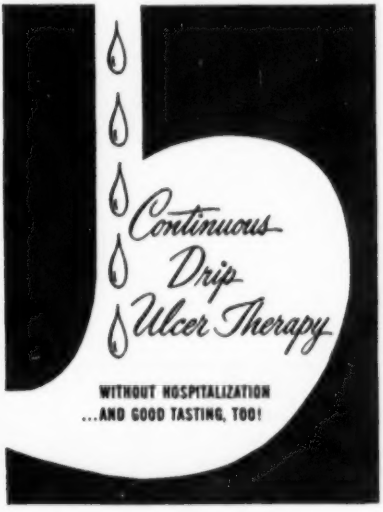
Hoelzel's observations with glass beads of different colors and their passage through the intestinal tract was not favorably received by gastroenterologists. The explanation given by Hoelzel, however, is that the different colors of glass beads produced by ingredients differing in specific gravity, may explain the differences in rate of passage.

The reviewer recalls these controversies, also the introduction in 1930 of celluflour, washed bran and food restriction for the prevention of intestinal toxemia.

This little book is interesting reading but adds nothing new to present day therapeutics.

DIAGNOSTIC ADVANCES IN GASTROINTESTINAL ROENTGENOLOGY: Arthur J. Bendick, M.D. 131 pages, 75 illustrations. Grune and Stratton, New York. 1954. Price $6.00.

The author is well known for his work on the roentgenological examination of the gastrointestinal tract. In 1948 he introduced the use of club soda to demonstrate pathology of the stomach and duodenum. His new book is written from personal ex-



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*Steigmann, F., and Goldberg, E.: Ambulatory Continuous Drip Method in the Treatment of Peptic Ulcer, Am. J. Digest. Dis. 22:67 (Mar.) 1955.

†Mg trisilicate 3.5 gr.; Ca carbonate 2.0 gr.; Mg oxide 2.0 gr.; Mg carbonate 0.5 gr.

perience, which he gained from many years of practice and as director of the roentgenological department of the Beth Israel Hospital in New York City.

Bendick gives a clear description of his technic, which is very thorough and enables the demonstration of the smallest pathological changes in the stomach and duodenum. All those who are not familiar with his work have to adjust themselves to read films taken after administration of club soda. He uses spot films extensively, which were thought to be harmful about 20 years ago. Examples of his films illustrate this well written book. We read it from cover to cover and have learned a great deal. The illustrations are very good, the index exhaustive. We can highly recommend the work to all those interested in gastroenterology and roentgenology, which means that the book will be read by many surgeons.

ANIMAL AGENTS AND VECTORS OF HUMAN DISEASE: E. C. Faust, M.A., Ph.D., William Vincent, Professor of Tropical Diseases and Hygiene and Head, Division of Parasitology, Department of Tropical Medicine and Public Health, Tulane University, New Orleans, La. 660 pages, 225 illustrations. Lea & Febiger, Philadelphia, Pa., 1955. Price $9.75.

Dr. Faust, although not a physician, is well known for his work in tropical medicine and this first edition dealing with animal agents and vectors covers the cause, symptoms, diagnosis, treatment and control of protozoa, roundworms, tapeworms, flukes, arthropods, and other animal forms.

An extensive authors' and subject index completes this well written and illustrated volume.

Public Health workers and others will find it a useful addition to their library.

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All copies of the March, 1954 issue of THE AMERICAN JOURNAL OF GASTROENTEROLOGY (Vol. 21, No. 3) addressed to foreign destinations were lost in the mails.

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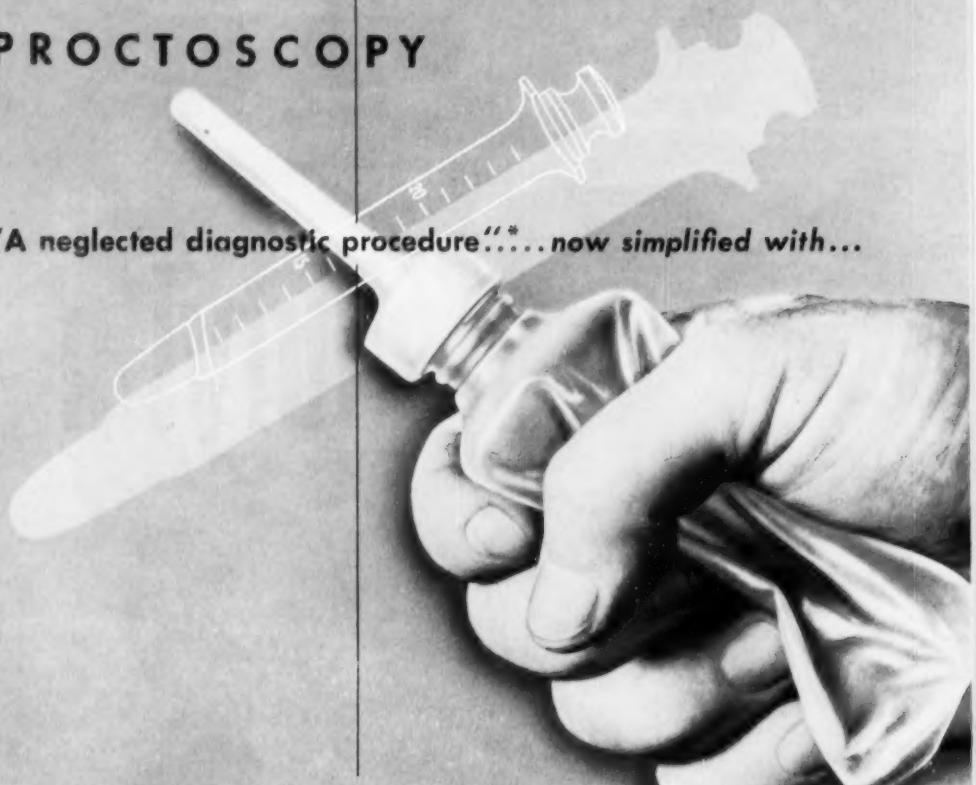

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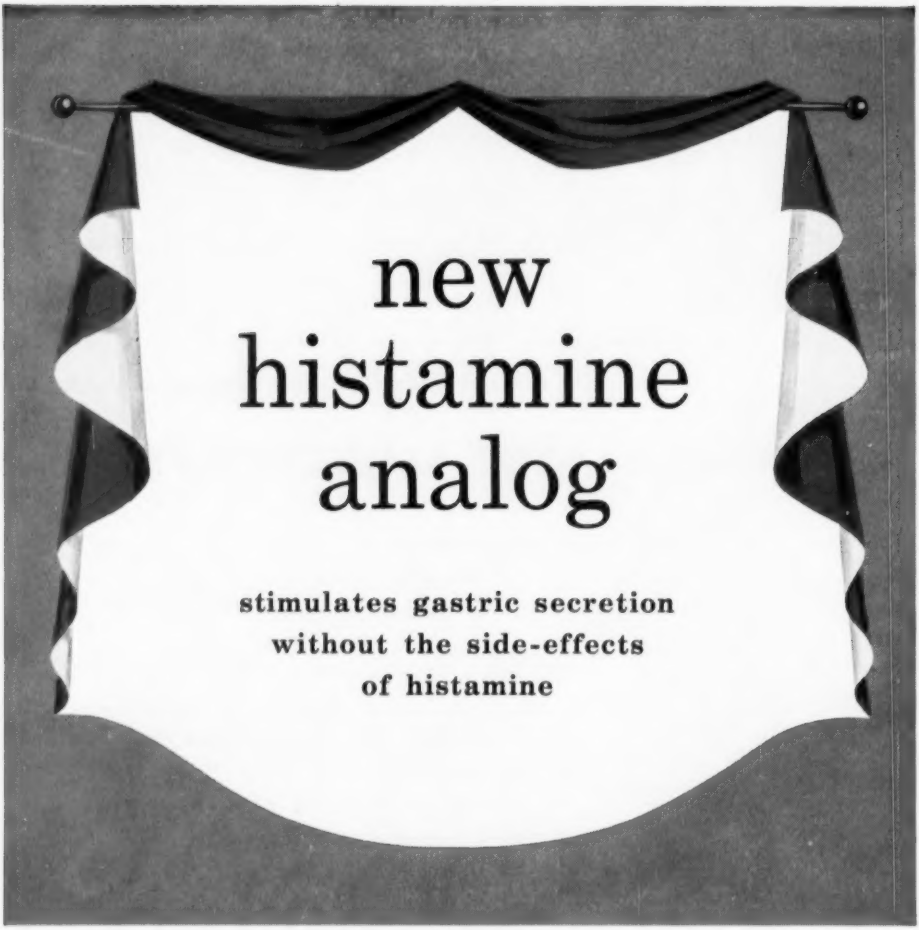
- Contains 2% Xylocaine Hydrochloride in an aqueous solution adjusted to a suitable consistency with carboxymethylcellulose. Cherry flavored for palatability.

Supplied: In bottles of 100 and 450 cc.
Average Dosage: One tablespoonful, administered orally.
Additional information available upon request

ASTRA

Astra Pharmaceutical Products, Inc., Worcester 6, Mass., U.S.A.

*U.S. Patent No. 2,441,498



Ampoules Histalog

Histalog, a new analog of histamine, selectively stimulates gastric secretion yet induces only a small fraction of the incidence of side-effects. Its vasodepressor action in animals is 1/700 that of histamine. In patients with a history of allergy, **Histalog** is especially indicated to avert serious flare-ups often caused by injection of histamine. Order a package of six ampoules from your local retail pharmacist. Complete dosage instructions are included in the package.

References

1. An Analog of Histamine That Stimulates Gastric Acid Secretion without Other Actions of Histamine, *Science*, *113*:651, 1951.
2. Gastric Secretory Response to 3-Beta Aminoethyl Pyrazole in Man, *Gastroenterology*, *20*:138, 1952.

Supplied as: **Ampoules Histalog,** 50 mg., 1 cc., in packages of 6 (No. 639).

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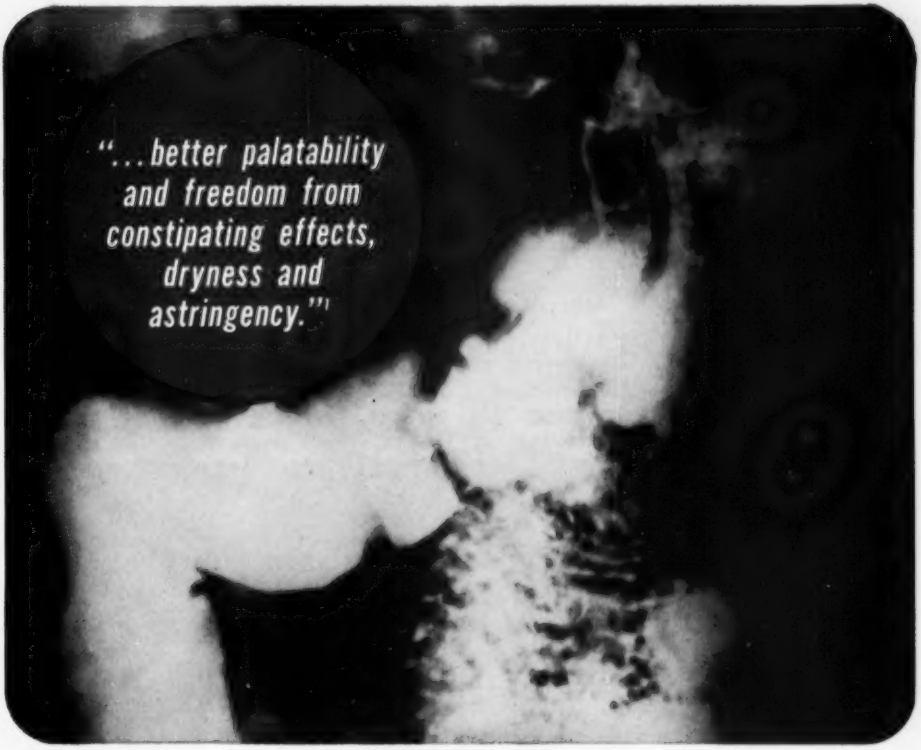

Morrison, in treating a large series of patients with Maalox-Rorer, describes this better-tolerated preparation as "... a palatable, antacid, demulcent, nonconstipating colloidal suspension of magnesium and aluminum hydroxides, useful for the relief of hyperacidity."

This clinician concludes: "Magnesium aluminum hydroxide gel is more palatable than aluminum hydroxide gel and better suited to the prolonged administration required for the antacid therapy of peptic ulcer and hyperchlorhydria."[1]

A well-balanced suspension, notable for its smooth texture and pleasant flavor, Maalox has gained remarkable patient acceptance.

maalox®
controls hyperacidity

Supplied: in 355 cc. (12 fluid ounce) bottles. In tablet form, bottles of 100. Each tablet equivalent to 1 fluidram of the suspension.

Samples sent promptly on request.

1. Morrison, Samuel: Magnesium aluminum hydroxide gel in the antacid therapy of peptic ulcer, Am. J. of Gastroenterology 22:309 (Oct.) 1954.

WILLIAM H. RORER, INC.
Philadelphia 6, Pa.

NOW PIPERIDOL ACTION

for peptic ulcer pain ⁊ spasm

cholinolytic

PIPTAL®

RELIEF DAY AND NIGHT

without urinary retention or

constipation

NORMALIZES GASTRIC MOTILITY AND SECRETION

Closely related to the visceral eutonic DACTIL®, PIPTAL curbs gastric hypermotility and duodenal spasm without significantly altering normal tonus or motility. A postganglionic parasympathetic inhibitor, cholinolytic PIPTAL normalizes gastric secretion, favors ulcer healing without undue interference with digestion.

WITHOUT URINARY RETENTION OR CONSTIPATION

Unlike compounds of other derivation, the effect of PIPTAL, latest LAKESIDE piperidol, is negligible on bladder and distal colon. Mydriasis, dryness of the mouth and tachycardia occur infrequently and are usually mild and transient. Side effects necessitating withdrawal of PIPTAL have not been observed.

cholinolytic

PIPTAL

Use the Patient Report Form accompanying mailed samples and see it work in your practice.

For relief day and night: One tablet T.I.D. and one or two H. S. Each tablet contains 5 mg. of PIPTAL, the *only* brand of N-ethyl-3-piperidyl -benzilate methobromide.

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Cremosuxidine®

SULFASUXIDINE® SUSPENSION WITH PECTIN AND KAOLIN

MAJOR ADVANTAGES: Has pronounced antibacterial action. Adsorbs and detoxifies intestinal irritants. Soothes the mucosa.

Adult dosage: 1½ to 2 tbsp. six times a day. *Pediatric dose* in proportion.

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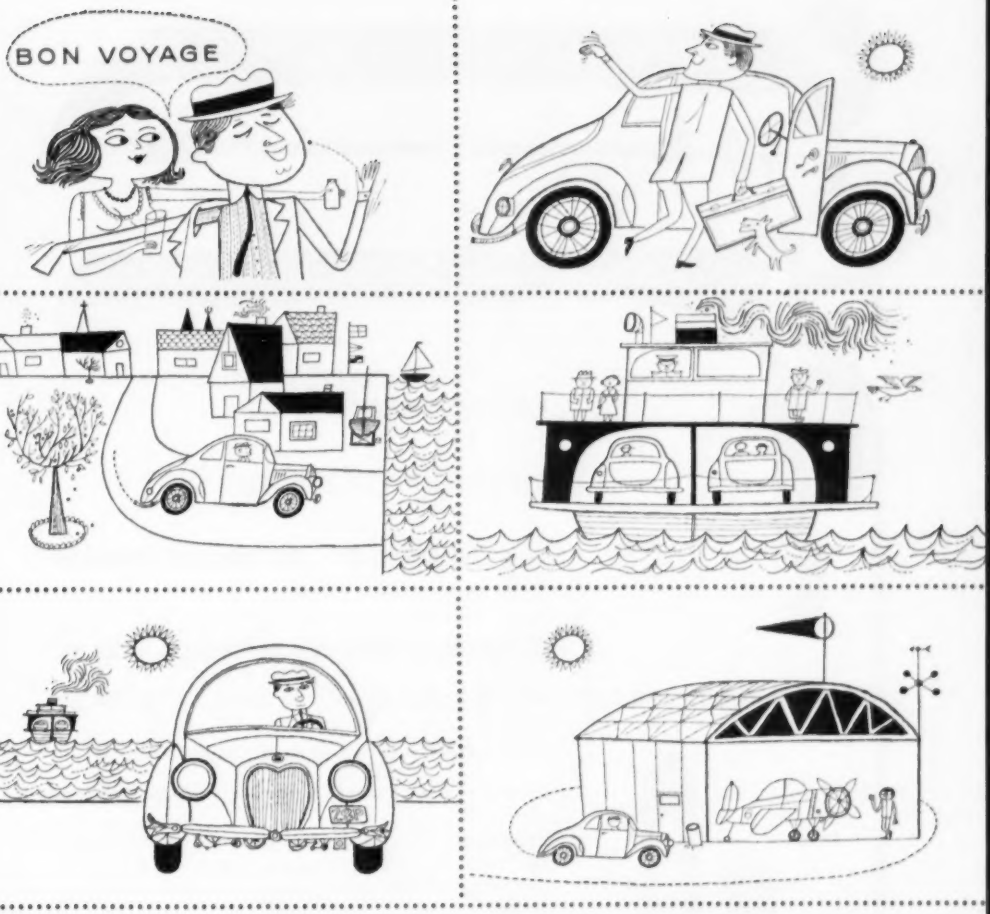
Once an idle minute was only a minute . . . until Coca-Cola put it to work for you. A pause for ice-cold Coca-Cola became the pause that refreshes—that little minute long enough for a big rest.

Coca-Cola, an honestly made product of an intrinsic quality, is a drink that performs a pleasant everyday service to millions in every walk of life.



. . . a comfortable voyage now assured with **Bonamine**®

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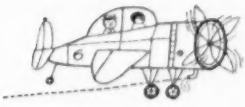

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Bonamine *is also useful in controlling the nausea, vomiting and vertigo associated with morning sickness of pregnancy, vestibular and labyrinthine disturbances, cerebral arteriosclerosis, radiation therapy and Menière's syndrome.*

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For complete information, consult your CIBA representative or write to Medical Service Division, CIBA, Summit, New Jersey.

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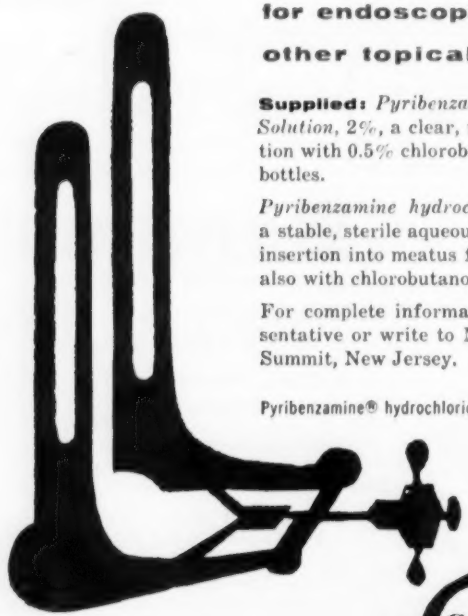

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the Resions

...specifics in diarrhea

The RESIONS offer two effective compounds for treatment of almost any diarrheal condition found in clinical practice.

The RESIONS act by ion exchange . . . to attract, bind and remove toxic materials in diarrheas caused by food or bacterial toxins; by prolonged use of certain drugs, and in general infectious diseases.

The RESIONS *are safe* because they are totally insoluble and non-toxic.

RESION therapy will control about 90% of common diarrheas.

RESION P-M-S is intended specifically for rapid control of those rare diarrheas caused by Gram-negative organisms; to prevent secondary bacterial infection; in mycotic diarrhea following the use of the broad-spectrum antibiotics, and to inhibit the enteric growth of *C. albicans* (Monilia).

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time-tested, adsorbent effectiveness

Polyamine methylene resin	10%
Sodium aluminum silicate	10%
Magnesium aluminum silicate	1.25%

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(Dysentery Fetish)

RESION *therapy now works scientific magic against diarrhea.*

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Resion P-M-S

A new formula providing antibacterials to combat bacillary and fungal vectors

NATIONAL

Each 15 cc. contains the RESION formula plus:

Polymyxin-B sulfate	125,000 units
Phthalylsulfacetamide	1.0 Gm.
Para hydroxy benzoic acid esters	0.235 Gm.

Dosage: RESION—1 tablespoonful hourly for 4 doses; then every 3 hours while awake. RESION P-M-S—1 tablespoonful hourly for 3 doses; then 3 times daily.

Supplied: RESION, in bottles of 4 and 12 fluid ounces. RESION P-M-S, bottles of 4 fl. oz.

THE NATIONAL DRUG COMPANY
Philadelphia 44, Pa.

Gastric Hyperacidity: etiology

People being people, environmental factors contributory to gastric hyperacidity are hard to remove, even when their role is clearly defined. But, the physician has a sure, simple—even pleasant—way of relieving the acid distress caused by:

- dietary indiscretion
- nervous tension
- emotional stress
- food intolerances
- excessive smoking
- alcoholic beverages

Gelusil promptly and effectively controls the excessive gastric acidity of "heartburn" and chronic indigestion. And it affords equally rapid relief in peptic ulcer. Sustained action is assured by combining magnesium trisilicate with the specially prepared aluminum hydroxide gel.

Free from constipation: Gelusil's aluminum hydroxide component is specially prepared: the concentration of aluminum ions is accordingly low; hence the formation of astringent—and constipating—aluminum chloride is minimal.

Free from acid rebound: Unlike soluble alkalies, Gelusil does not over-neutralize or alkalinize. It maintains the gastric pH in a mildly acid range—that of maximum physiologic functioning.

Dosage—2 tablets or 2 teaspoonfuls two hours after eating or when symptoms are pronounced. Each tablet or teaspoonful provides: 7½ gr. magnesium trisilicate and 4 gr. aluminum hydroxide gel.

Available—Gelusil Tablets in packages of 50, 100, 1000 and 5000. Gelusil Liquid in bottles of 6 and 12 fluidounces.

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Antacid • Adsorbent

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